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IBD-RELATED POLYMORPHISMS

RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Serial No. 60/170,257, filed December 10, 1999, and U.S. Provisional Application Serial No. 5 60/196,046, filed April 10, 2000, the entire teachings of both of which are incorporated herein by reference in their entirety.

BACKGROUND OF THE INVENTION

The genomes of all organisms undergo spontaneous mutation in the course of their continuing evolution, generating variant forms of progenitor nucleic acid sequences (Gusella, *Ann. Rev. Biochem.* 55, 831-854 (1986)). The variant form may confer an evolutionary advantage or disadvantage relative to a progenitor form, or may be neutral. In some instances, a variant form confers a lethal disadvantage and is not transmitted to subsequent generations of the organism. In other instances, a variant form confers an evolutionary advantage to the species and is eventually incorporated into the DNA of many or most members of the species and effectively becomes the

progenitor form. In many instances, both progenitor and variant form(s) survive and co-exist in a species population. The coexistence of multiple forms of a sequence gives rise to polymorphisms.

Several different types of polymorphism have been reported. A restriction
5 fragment length polymorphism (RFLP) is a variation in DNA sequence that alters the length of a restriction fragment (Botstein *et al.*, *Am. J. Hum. Genet.* 32, 314-331 (1980)). The restriction fragment length polymorphism may create or delete a restriction site, thus changing the length of the restriction fragment. RFLPs have been widely used in human and animal genetic analyses (see WO 90/13668; W090/11369;
10 Donis-Keller, *Cell* 51, 319-337 (1987); Lander *et al.*, *Genetics* 121, 85-99 (1989)). When a heritable trait can be linked to a particular RFLP, the presence of the RFLP in an individual can be used to predict the likelihood that the animal will also exhibit the trait.

Other polymorphisms take the form of short tandem repeats (STRs) that include
15 tandem di-, tri- and tetra-nucleotide repeated motifs. These tandem repeats are also referred to as variable number tandem repeat (VNTR) polymorphisms. VNTRs have been used in identity and paternity analysis (US 5,075,217; Armour *et al.*, *FEBS Lett.* 307, 113-115 (1992); Horn *et al.*, W0 91/14003; Jeffreys, EP 370,719), and in a large number of genetic mapping studies.

20 Other polymorphisms take the form of single nucleotide variations between individuals of the same species. Such polymorphisms are far more frequent than RFLPs, STRs and VNTRs. Some single nucleotide polymorphisms (SNP) occur in protein-coding nucleic acid sequences (coding sequence SNP (cSNP)), in which case, one of the polymorphic forms may give rise to the expression of a defective or otherwise
25 variant protein and, potentially, a genetic disease. Examples of genes in which polymorphisms within coding sequences give rise to genetic disease include β -globin (sickle cell anemia), apoE4 (Alzheimer's Disease), Factor V Leiden (thrombosis), and CFTR (cystic fibrosis). cSNPs can alter the codon sequence of the gene and therefore specify an alternative amino acid. Such changes are called "missense" when another

amino acid is substituted, and "nonsense" when the alternative codon specifies a stop signal in protein translation. When the cSNP does not alter the amino acid specified the cSNP is called "silent". Other single nucleotide polymorphisms occur in noncoding regions. Some of these polymorphisms may also result in defective protein expression (e.g., as a result of defective splicing). Other single nucleotide polymorphisms have no phenotypic effects.

Single nucleotide polymorphisms can be used in the same manner as RFLPs and VNTRs, but offer several advantages. Single nucleotide polymorphisms occur with greater frequency and are spaced more uniformly throughout the genome than other forms of polymorphism. The greater frequency and uniformity of single nucleotide polymorphisms means that there is a greater probability that such a polymorphism will be found in close proximity to a genetic locus of interest than would be the case for other polymorphisms. The different forms of characterized single nucleotide polymorphisms are often easier to distinguish than other types of polymorphism (e.g., by use of assays employing allele-specific hybridization probes or primers).

Only a small percentage of the total repository of polymorphisms in humans and other organisms has been identified. The limited number of polymorphisms identified to date is due to the large amount of work required for their detection by conventional methods. For example, a conventional approach to identifying polymorphisms might be to sequence the same stretch of DNA in a population of individuals by dideoxy sequencing. In this type of approach, the amount of work increases in proportion to both the length of sequence and the number of individuals in a population and becomes impractical for large stretches of DNA or large numbers of persons.

SUMMARY OF THE INVENTION

Work described herein pertains to the identification of polymorphisms which are associated with inflammatory bowel diseases (IBD), and particularly those within a single risk haplotype, by resequencing large numbers of genes and gene fragments in a large number of individuals. Various genes from a number of individuals have been

resequenced as described herein, and SNPs in these genes have been discovered (see Table 3). Some of these SNPs are cSNPs which specify a different amino acid sequence, some of the SNPs are silent cSNPs and some of these cSNPs specify a stop signal in protein translation. Some of the identified SNPs were located in non-coding regions.

With the goal of identifying IBD susceptibility genes, a genomewide scan was undertaken in 163 pedigrees, and three regions of suggestive linkage (3, 5q31-33, 6p) and one of significant linkage to 19p13 (LOD = 4.6) were identified. Higher density mapping in the suggestive 5q31-33 region revealed a CD susceptibility locus of genome-wide significance (LOD = 3.9). Importantly, the 5q31-p33 localizes to the major immunoregulatory cytokine gene cluster and the 19p13 locus to a region containing numerous genes encoding cytokine/chemokine receptors and other inflammatory-associated molecules that could have a direct role in disease susceptibility.

In order to pursue the evidence of linkage to chromosome 5, a systematic linkage disequilibrium (LD) approach was adopted. The approach that was used in the first stage of LD mapping was to genotype all known microsatellite markers in the 18 cM between D5S1435 and D5S1480, as these two markers delimit a region of a 2 LOD drop on either side of the linkage peak centered at marker D5S2497. All alleles for each marker were examined for evidence of excess transmission from heterozygous parents to CD child using the transmission disequilibrium test (TDT). Only alleles at two of the 57 markers had significant C^2 results ($p < 0.001$): IRF1p1 ($C^2 = 13.3$, $p = 0.0003$) and D5S1984 ($C^2 = 14.0$, $p = 0.0002$) (Table 1). A second stage of mapping was then undertaken to confirm, as well as to better delimit, the region of LD surrounding IRF1p1 and D5S1984. The development of new microsatellite markers was necessary. The marker with the most significant C^2 result was CAh17a ($C^2 = 16.2$, $p = 0.00006$) and was located between IRF1p1 and D5S1984 (Table 2). Furthermore, the alleles 193, 156, 373, 140, 222, and 307 at markers GAh18a, IRF1p, CAh15a, CAh17a, D5S1984,

CSF2p10, respectively, define a haplotype conferring susceptibility to Crohn's disease (CD). In order to identify the sequence variant that would explain the genetic susceptibility to CD provided by this haplotype, a search was performed for all single nucleotide polymorphisms (SNPs) in this region of LD. The SNP discovery was
 5 accomplished by direct sequencing of overlapping PCR products amplified from DNA samples from eight individuals (six CD patients, one unaffected family member, and one CEPH DNA as control). Table 3 shows the results of the SNP discovery analyses.

139 triads were genotyped for a total of 241 SNPs thus far, where at least 50 trios were fully genotyped. Using a C^2 value of 13 (corresponding to a p-value of 0.05) as
 10 threshold, 12 SNPs were found to have a significant level of association with CD and extended over a region of 250 kb, from IRF1 to prolyl4 hydroxylase. These were markers IGR2055a_1, IGR2060a_1, IGR2063b_1, IGR2069a_2, IGR2078a_1, IGR2096a_1, IGR2198a_1, IGR2230a_1, IGR2277a_1, IGR3081a_1, IGR3096a_1, PROLYLex3_1 (see Table 4). Any of these best SNPs by themselves are in strong
 15 association with CD and fully explain the microsatellite LD observations. Furthermore, the best SNPs have nearly identical association characteristics (that is, the allele at one SNP determines the allele of all others on any phased chromosome), confirming that a single risk haplotype extending approximately 250 kb is the source of all the observations of association in this region. Specifically, this haplotype is defined by the
 20 alleles G, C, G, T, A, A, G, T, G, G, C, T at markers IGR2055a_1, IGR2060a_1, IGR2063b_1, IGR2069a_2, IGR2078a_1, IGR2096a_1, IGR2198a_1, IGR2230a_1, IGR2277a_1, IGR3081a_1, IGR3096a_1, PROLYLex3_1, respectively. The frequency of this haplotype is estimated to be approximately 37% in the general population. Furthermore, this haplotype is transmitted from heterozygous parents to CD patients at a
 25 ratio of 2.5:1.

The invention relates to a isolated gene or nucleic acid molecule which comprises a single nucleotide polymorphism at a specific location. In a particular embodiment the invention relates to the variant allele of a gene having a single nucleotide polymorphism, which variant allele differs from a reference allele by one nucleotide at

the site(s) identified in Table 3. Complements of these nucleic acid segments are also included. The segments can be DNA or RNA, and can be double- or single-stranded. Segments can be, for example, 5-10, 5-15, 10-20, 5-25, 10-30, 10-50 or 10-100 bases long.

- 5 The invention further provides allele-specific oligonucleotides that hybridize to a gene comprising a single nucleotide polymorphism or to the complement of the gene. These oligonucleotides can be probes or primers.

- 10 The invention further provides a method of analyzing a nucleic acid from an individual. The method determines which base is present at any one of the polymorphic sites shown in Table 3. Optionally, a set of bases occupying a set of the polymorphic sites shown in Table 3 is determined. This type of analysis can be performed on a number of individuals, who are tested for the presence of a disease phenotype. The presence or absence of disease phenotype is then correlated with a base or set of bases present at the polymorphic site or sites in the individuals tested.

- 15 Thus, the invention further relates to a method of predicting the presence, absence, likelihood of the presence or absence, or severity of a particular phenotype or disorder associated with a particular genotype. The method comprises obtaining a nucleic acid sample from an individual and determining the identity of one or more bases (nucleotides) at polymorphic sites of genes described herein, wherein the presence of a particular base is correlated with a specified phenotype or disorder, thereby predicting the presence, absence, likelihood of the presence or absence, or severity of the phenotype or disorder in the individual. In one embodiment of the invention, the phenotype is inflammatory bowel disease or Crohn's disease.

BRIEF DESCRIPTION OF THE DRAWING

- 25 The Figure shows multipoint nonparametric linkage results for the IBD genome scan. Multipoint LOD scores were calculated using the MAPMAKER/SIBS functions implemented in GENHUNTER 2.0. The thick black line indicates the LOD score along the length of each chromosome, and the tick marks indicate the position of the

microsatellite markers. The two horizontal lines depict the genome-wide thresholds for suggestive (LOD = 2.0) and significant linkage.

DETAILED DESCRIPTION OF THE INVENTION

- Crohn's disease (CD) and ulcerative colitis (UC) are chronic, idiopathic inflammatory disorders of the gastrointestinal tract. These inflammatory bowel diseases (IBD) have a peak incidence in early adulthood, and their combined prevalence is approximately 100-200/100,000. The inflammation in IBD is characterized by altered expression of both pro-inflammatory and immunoregulatory cytokines in the affected intestinal mucosa (Kmiec, *Arch Immunol Ther Expe (Warsz)* 46(3):143-155 (1998)).
- Genetic factors are believed to play an important role, as the sibling risk (λ_s) calculated for IBD ranges from 15-40, with a stronger genetic contribution occurring for CD ($\lambda_s \sim 35$) as compared to UC ($\lambda_s \sim 15$). Additionally, relatives of individuals with IBD diagnosed at younger ages appear to be at an even higher risk.
- CD is characterized by discontinuous, transmural inflammation affecting any part of the gastrointestinal tract and is manifested by abdominal pain, chronic diarrhea, weight loss, bowel obstructions and fistulae. UC occurs as a continuous, mucosal inflammation affecting only the large intestine with primary symptoms including diarrhea, rectal bleeding and abdominal pain. The search for susceptibility genes for these two diseases has resulted in the identification of two potential susceptibility loci.
- The first, called *IBD1*, is a CD-susceptibility locus that lies in the pericentromeric region of chromosome 16 (Hugo *et al.*, *Nature* 379:821-822 (1996)). The second (*IBD2*) is located in a 41 cM region surrounding marker D12S83 and appears to be linked to both CD and UC (Satsangi *et al.*, *Genetics* 14:199-202 (1996)). These putative loci, however, have only been replicated in some, but not all, subsequent studies (Cavanaugh *et al.*, *Proc Natl Acad Sci USA* 62:291-298 (1998); Cho *et al.*, *The National Academy of Sciences* 95:7502-7507 (1998); Curren *et al.*, *Gastroenterology* 115:1-7 (1998); Duerr *et al.*, *The American Society of Human Genetics* 63:95-100 (1998); Rioux *et al.*, *Am. J. Hum. Genet.* 63:1086-1094 (1998); Yang *et al.*,

Gastroenterology 109:440-448 (1995)), supporting the belief that there exists substantial genetic heterogeneity. Furthermore, *IBD1* and *IBD2* only account for a fraction of the heritability of IBD, suggesting that additional loci contribute to disease susceptibility. Thus, as described herein, the susceptibility loci in a Canadian IBD

5 population was assessed by studying families with multiple affected siblings (McLeod *et al.*, *Dis Colon Rectum* 40:553-557 (1997)).

A genome-wide screen was performed on 181 IBD-affected sibling pairs (ASP) and 5 IBD-affected relative pairs (RP) from 163 families. Among these ASP, 122 were CD pairs, 25 were UC pairs, and 34 were “mixed” pairs (one sibling with either CD or

10 UC, the other with CD, UC or IC). All ASP and available parents (140 families had both parents available, 17 had one parent available, and 1 was missing both parents), as well as all RP, were genotyped with 312 microsatellite markers covering the genome with approximately 12 cM distance between markers. Simulations of this dataset indicated that the genome-wide threshold for suggestive linkage (the score expected to

15 occur one time at random in a genome scan) was at a LOD of 2.0. Using either this calculated threshold, or the published threshold of LOD 2.2 based on an infinitely dense map (Lander & Kruglyak, *Nature Genetics* 11:241-247 (1995)), multipoint nonparametric linkage analysis of these data revealed 4 loci which surpassed this threshold (Figure). Specifically, chromosome 3 had a peak LOD of 2.4 between

20 markers D3S1766 and D#S1285, chromosome 5 a peak LOD of 3.0 between GATA68A03 and D5S816, chromosome 6 a peak LOD of 2.3 between D6S1019 and D6S1017, and chromosome 19 a peak LOD of 4.6 between GATA21G05 and D19S586. In fact this chromosome 19 locus exceeds the threshold for genome-wide significance of 3.6 (Lander & Kruglyak, *Nature Genetics* 11:241-247 (1995)), and represents a novel

25 IBD susceptibility locus.

This novel locus maps to an extended region on 19p13 (Figure) that contains many different genes of immunologic interest such as intercellular adhesion molecule 1 (ICAM1), complement component 3 (C3), the thromboxane A2 receptor (TBXA2), leukotriene B4 hydroxylase (LTB4H), and the janus tyrosine kinases TYK2 and JAK3.

There is some evidence supporting their relevance in IBD susceptibility: 1) modest positive association results have been reported for the ICAM1 (Yang *et al.*, *Gastroenterology* 109:440-448 (1995)) and C3 molecules (Elmgreen *et al.*, *Acta Med Scand* 215(4):375-8 (1984)); 2) attempts to interfere with the TBXA2 (Taniguchi, 1997) and LTB4 (Hawkey *et al.*, *Agents Actions, Special Conference Issue* (1992)) mediated inflammatory pathways have shown some therapeutic value; and 3) the janus kinases have been shown to be important in the transduction of the molecular signal from cytokine receptors.

The finding of suggestive linkage to an approximately 30 cM region spanning the cytokine gene cluster on 5q31-q33, containing many of the immunoregulatory cytokines such as IL4, IL13, IL5 and IL3, led to the performance of higher density mapping in this region. Specifically, the original families and an additional 12 families were genotyped for 34 extra microsatellite markers. Multipoint nonparametric analysis were then performed using three different phenotypic categories: IBD, CD and CD16. In the first, all individuals with CD, UC or IC were designated as affected; in the second, only individuals with CD were designated as affected; in the third, only individuals with CD were designated as affected and only families with at least one affected sibling diagnosed at the age of 16 or younger were included. This last category was examined due to an expected enrichment for genetic factors over environmental causes. These analyses demonstrate the presence of a locus of genome-wide significance in the group with early onset CD (MLS = 3.9). Evidence for linkage to the syntenic region in mice has been reported in an induced model of colitis (Mahler, *Genomics* 55:147-156 (1999)).

Although the suggestive loci on chromosomes 3 and 6 identified as described herein have not yet been followed up with higher density mapping, it is important to note that the linkage peak on chromosome 3 is approximately 10 cM away from a previously reported suggestive locus (Satsangi *et al.*, *Nature Genetics* 14:199-202 (1996)), and the linkage peak on 6 lies approximately 20 cM centromeric to the major histocompatibility complex (MHC) Class II region. A recent study has described

linkage to this chromosome 6 region (Hampe *et al.*, *Am. J. Hum. Genet.* 64 (1999)), and a large meta-analysis of the results derived from 29 different studies has also reported that both CD and UC were associated with specific Class II alleles (Stokkers *et al.*, *Gut* 45:395-401 (1999)). Finally, in order to assess whether the *IBD1* and *IBD2* loci are contributing to the IBD susceptibility in this population, exclusion mapping of the data was performed. These analyses demonstrate that the entire chromosome 12 can be excluded for loci of even modest effects ($\lambda_s > 1.5$), but can only loci conferring a $\lambda_s > 4$ on chromosome 16 can be excluded, suggesting that *IBD1* ($\lambda_s \sim 1.3$) could have gone undetected in the present study.

Thus, this work has identified two novel susceptibility loci: a locus on chromosome 5q31-33 that confers susceptibility to CD and a locus on chromosome 19p13 that confers susceptibility to IBD. Furthermore, particular SNPs within these loci have been identified which may be associated with disease susceptibility.

The present invention relates to a gene which comprises a single nucleotide polymorphism (SNP) at a specific location. The gene which includes the SNP has at least two alleles, referred to herein as the reference allele and the variant allele. The reference allele (prototypical or wild type allele) has been designated arbitrarily and typically corresponds to the nucleotide sequence of the gene which has been deposited with GenBank or TIGR under a given Accession number. The variant allele differs from the reference allele by one nucleotide at the site(s) identified in Table 3. The present invention also relates to variant alleles of the described genes and to complements of the variant alleles. The invention further relates to portions of the variant alleles and portions of complements of the variant alleles which comprise (encompass) the site of the SNP and are at least 5 nucleotides in length. Portions can be, for example, 5-10, 5-15, 10-20, 5-25, 10-30, 10-50 or 10-100 bases long. For example, a portion of a variant allele which is 21 nucleotides in length includes the single nucleotide polymorphism (the nucleotide which differs from the reference allele at that site) and twenty additional nucleotides which flank the site in the variant allele. These nucleotides can be on one or both sides of the polymorphism.

Polymorphisms which are the subject of this invention are defined in Table 3. The reference sequence for many of the genes or gene fragments is provided in Table 5. For sequences which are not present in Table 5, the skilled artisan can readily determine the specific location of the polymorphism given the 3' and 5' nucleotide sequence

5 flanking the polymorphic site provided in Table 3 and the chromosomal loci information provided herein. The nucleotide sequences of the invention can be double- or single-stranded.

The invention further provides allele-specific oligonucleotides that hybridize to a gene comprising a single nucleotide polymorphism or to the complement of the gene.

10 These oligonucleotides can be probes or primers.

The invention further provides a method of analyzing a nucleic acid from an individual. The method determines which base is present at any one of the polymorphic sites shown in Table 3. Optionally, a set of bases occupying a set of the polymorphic sites shown in Table 3 is determined. This type of analysis can be performed on a
15 number of individuals, who are tested for the presence of a disease phenotype. The presence or absence of disease phenotype is then correlated with a base or set of bases present at the polymorphic site or sites in the individuals tested.

Thus, the invention further relates to a method of predicting the presence, absence, likelihood of the presence or absence, or severity of a particular phenotype or disorder associated with a particular genotype. The method comprises obtaining a nucleic acid
20 sample from an individual and determining the identity of one or more bases (nucleotides) at polymorphic sites of genes described herein, wherein the presence of a particular base is correlated with a specified phenotype or disorder, thereby predicting the presence, absence, likelihood of the presence or absence, or severity of the
25 phenotype or disorder in the individual.

DEFINITIONS

An oligonucleotide can be DNA or RNA, and single- or double-stranded. Oligonucleotides can be naturally occurring or synthetic, but are typically prepared by

synthetic means. Preferred oligonucleotides of the invention include segments of DNA, or their complements, which include any one of the polymorphic sites shown in Table 3. The segments can be between 5 and 250 bases, and, in specific embodiments, are between 5-10, 5-20, 10-20, 10-50, 20-50 or 10-100 bases. For example, the segment
5 can be 21 bases. The polymorphic site can occur within any position of the segment. The segments can be from any of the allelic forms of DNA shown in Table 3.

As used herein, the terms "nucleotide", "base" and "nucleic acid" are intended to be equivalent. The terms "nucleotide sequence", "nucleic acid sequence", "nucleic acid molecule" and "segment" are intended to be equivalent.

10 Hybridization probes are oligonucleotides which bind in a base-specific manner to a complementary strand of nucleic acid. Such probes include peptide nucleic acids, as described in Nielsen *et al.*, *Science* 254, 1497-1500 (1991). Probes can be any length suitable for specific hybridization to the target nucleic acid sequence. The most appropriate length of the probe may vary depending upon the hybridization method in
15 which it is being used; for example, particular lengths may be more appropriate for use in microfabricated arrays, while other lengths may be more suitable for use in classical hybridization methods. Such optimizations are known to the skilled artisan. Suitable probes and primers can range from about 5 nucleotides to about 30 nucleotides in length. For example, probes and primers can be 5, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24,
20 25, 26, 28 or 30 nucleotides in length. The probe or primer preferably overlaps at least one polymorphic site occupied by any of the possible variant nucleotides. The nucleotide sequence can correspond to the coding sequence of the allele or to the complement of the coding sequence of the allele.

As used herein, the term "primer" refers to a single-stranded oligonucleotide
25 which acts as a point of initiation of template-directed DNA synthesis under appropriate conditions (*e.g.*, in the presence of four different nucleoside triphosphates and an agent for polymerization, such as DNA or RNA polymerase or reverse transcriptase) in an appropriate buffer and at a suitable temperature. The appropriate length of a primer depends on the intended use of the primer, but typically ranges from 15 to 30

nucleotides. Short primer molecules generally require cooler temperatures to form sufficiently stable hybrid complexes with the template. A primer need not reflect the exact sequence of the template, but must be sufficiently complementary to hybridize with a template. The term primer site refers to the area of the target DNA to which a primer hybridizes. The term primer pair refers to a set of primers including a 5' (upstream) primer that hybridizes with the 5' end of the DNA sequence to be amplified and a 3' (downstream) primer that hybridizes with the complement of the 3' end of the sequence to be amplified.

As used herein, linkage describes the tendency of genes, alleles, loci or genetic markers to be inherited together as a result of their location on the same chromosome. It can be measured by percent recombination between the two genes, alleles, loci or genetic markers.

As used herein, polymorphism refers to the occurrence of two or more genetically determined alternative sequences or alleles in a population. A polymorphic marker or site is the locus at which divergence occurs. Preferred markers have at least two alleles, each occurring at frequency of greater than 1%, and more preferably greater than 10% or 20% of a selected population. A polymorphic locus may be as small as one base pair. Polymorphic markers include restriction fragment length polymorphisms, variable number of tandem repeats (VNTR's), hypervariable regions, minisatellites, dinucleotide repeats, trinucleotide repeats, tetranucleotide repeats, simple sequence repeats, and insertion elements such as Alu. The first identified allelic form is arbitrarily designated as the reference form and other allelic forms are designated as alternative or variant alleles. The allelic form occurring most frequently in a selected population is sometimes referred to as the wildtype form. Diploid organisms may be homozygous or heterozygous for allelic forms. A diallelic or biallelic polymorphism has two forms. A triallelic polymorphism has three forms.

Work described herein pertains to the resequencing of large numbers of genes in a large number of individuals to identify polymorphisms which can predispose individuals to disease, particularly IBD.

By altering amino acid sequence, SNPs may alter the function of the encoded proteins. The discovery of the SNP facilitates biochemical analysis of the variants and the development of assays to characterize the variants and to screen for pharmaceutical that would interact directly with on or another form of the protein. SNPs (including
5 silent SNPs) may also alter the regulation of the gene at the transcriptional or post-transcriptional level. SNPs (including silent SNPs) also enable the development of specific DNA, RNA, or protein-based diagnostics that detect the presence or absence of the polymorphism in particular conditions.

A single nucleotide polymorphism occurs at a polymorphic site occupied by a
10 single nucleotide, which is the site of variation between allelic sequences. The site is usually preceded by and followed by highly conserved sequences of the allele (e.g., sequences that vary in less than 1/100 or 1/1000 members of the populations).

A single nucleotide polymorphism usually arises due to substitution of one nucleotide for another at the polymorphic site. A transition is the replacement of one
15 purine by another purine or one pyrimidine by another pyrimidine. A transversion is the replacement of a purine by a pyrimidine or vice versa. Single nucleotide polymorphisms can also arise from a deletion of a nucleotide or an insertion of a nucleotide relative to a reference allele. Typically the polymorphic site is occupied by a base other than the reference base. For example, where the reference allele contains the
20 base "T" at the polymorphic site, the altered allele can contain a "C", "G" or "A" at the polymorphic site.

Hybridizations are usually performed under stringent conditions, for example, at a salt concentration of no more than 1 M and a temperature of at least 25°C. For example, conditions of 5X SSPE (750 mM NaCl, 50 mM NaPhosphate, 5 mM EDTA,
25 pH 7.4) and a temperature of 25-30°C, or equivalent conditions, are suitable for allele-specific probe hybridizations. Equivalent conditions can be determined by varying one or more of the parameters given as an example, as known in the art, while maintaining a similar degree of identity or similarity between the target nucleotide sequence and the primer or probe used.

The term "isolated" is used herein to indicate that the material in question exists in a physical milieu distinct from that in which it occurs in nature. For example, an isolated nucleic acid of the invention may be substantially isolated with respect to the complex cellular milieu in which it naturally occurs. In some instances, the isolated material will form part of a composition (for example, a crude extract containing other substances), buffer system or reagent mix. In other circumstance, the material may be purified to essential homogeneity, for example as determined by PAGE or column chromatography such as HPLC. Preferably, an isolated nucleic acid comprises at least about 50, 80 or 90 percent (on a molar basis) of all macromolecular species present.

10 I. Novel Polymorphisms of the Invention

The novel polymorphisms of the invention are shown in Table 3.

II. Analysis of Polymorphisms

A. Preparation of Samples

Polymorphisms are detected in a target nucleic acid from an individual being analyzed. For assay of genomic DNA, virtually any biological sample (other than pure red blood cells) is suitable. For example, convenient tissue samples include whole blood, semen, saliva, tears, urine, fecal material, sweat, buccal, skin and hair. For assay of cDNA or mRNA, the tissue sample must be obtained from an organ in which the target nucleic acid is expressed. For example, if the target nucleic acid is a cytochrome P450, the liver is a suitable source.

Many of the methods described below require amplification of DNA from target samples. This can be accomplished by e.g., PCR. *See generally PCR Technology: Principles and Applications for DNA Amplification* (ed. H.A. Erlich, Freeman Press, NY, NY, 1992); *PCR Protocols: A Guide to Methods and Applications* (eds. Innis, et al., Academic Press, San Diego, CA, 1990); Mattila *et al.*, *Nucleic Acids Res.* 19, 4967 (1991); Eckert *et al.*, *PCR Methods and Applications* 1, 17 (1991); PCR (eds. McPherson *et al.*, IRL Press, Oxford); and U.S. Patent 4,683,202.

Other suitable amplification methods include the ligase chain reaction (LCR) (see Wu and Wallace, *Genomics* 4, 560 (1989), Landegren *et al.*, *Science* 241, 1077 (1988), transcription amplification (Kwoh *et al.*, *Proc. Natl. Acad. Sci. USA* 86, 1173 (1989)), and self-sustained sequence replication (Guatelli *et al.*, *Proc. Nat. Acad. Sci. USA*, 87, 1874 (1990)) and nucleic acid based sequence amplification (NASBA). The latter two
5 amplification methods involve isothermal reactions based on isothermal transcription, which produce both single stranded RNA (ssRNA) and double stranded DNA (dsDNA) as the amplification products in a ratio of about 30 or 100 to 1, respectively.

B. Detection of Polymorphisms in Target DNA

10 The polymorphisms identified as described herein can be used as a platform for genotyping (i.e., determining the genotype of) individuals. This analysis determines which form(s) of a characterized (known) polymorphism are present in individuals under test. There are a variety of suitable procedures, which are discussed in turn.

1. Allele-Specific Probes

15 The design and use of allele-specific probes for analyzing polymorphisms is described by e.g., Saiki *et al.*, *Nature* 324, 163-166 (1986); Dattagupta, EP 235,726, Saiki, WO 89/11548. Allele-specific probes can be designed that hybridize to a segment of target DNA from one individual but do not hybridize to the corresponding segment from another individual due to the presence of different polymorphic forms in
20 the respective segments from the two individuals. Hybridization conditions should be sufficiently stringent that there is a significant difference in hybridization intensity between alleles, and preferably an essentially binary response, whereby a probe hybridizes to only one of the alleles. Some probes are designed to hybridize to a segment of target DNA such that the polymorphic site aligns with a central position
25 (e.g., in a 15-mer at the 7 position; in a 16-mer, at either the 8 or 9 position) of the probe. This design of probe achieves good discrimination in hybridization between different allelic forms.

Allele-specific probes are often used in pairs, one member of a pair showing a perfect match to a reference form of a target sequence and the other member showing a perfect match to a variant form. Several pairs of probes can then be immobilized on the same support for simultaneous analysis of multiple polymorphisms within the same target sequence.

2. Tiling Arrays

The polymorphisms can also be identified by hybridization to nucleic acid arrays, some examples of which are described in WO 95/11995. One form of such arrays is described in the Examples section in connection with de novo identification of polymorphisms. The same array or a different array can be used for analysis of characterized polymorphisms. WO 95/11995 also describes subarrays that are optimized for detection of a variant form of a precharacterized polymorphism. Such a subarray contains probes designed to be complementary to a second reference sequence, which is an allelic variant of the first reference sequence. The second group of probes is designed by the same principles as described in the Examples, except that the probes exhibit complementarity to the second reference sequence. The inclusion of a second group (or further groups) can be particularly useful for analyzing short subsequences of the primary reference sequence in which multiple mutations are expected to occur within a short distance commensurate with the length of the probes (e.g., two or more mutations within 9 to 21 bases).

3. Allele-Specific Primers

An allele-specific primer hybridizes to a site on target DNA overlapping a polymorphism and only primes amplification of an allelic form to which the primer exhibits perfect complementarity. See Gibbs, *Nucleic Acid Res.* 17, 2427-2448 (1989). This primer is used in conjunction with a second primer which hybridizes at a distal site. Amplification proceeds from the two primers, resulting in a detectable product which indicates the particular allelic form is present. A control is usually performed with a

second pair of primers, one of which shows a single base mismatch at the polymorphic site and the other of which exhibits perfect complementarity to a distal site. The single-base mismatch prevents amplification and no detectable product is formed. The method works best when the mismatch is included in the 3'-most position of the oligonucleotide aligned with the polymorphism because this position is most destabilizing to elongation from the primer (see, e.g., WO 93/22456).

4. Direct-Sequencing

The direct analysis of the sequence of polymorphisms of the present invention can be accomplished using either the dideoxy chain termination method or the Maxam - Gilbert method (see Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual* (2nd Ed., CSHP, New York 1989); Zyskind *et al.*, *Recombinant DNA Laboratory Manual*, (Acad. Press, 1988)).

5. Denaturing Gradient Gel Electrophoresis

Amplification products generated using the polymerase chain reaction can be analyzed by the use of denaturing gradient gel electrophoresis. Different alleles can be identified based on the different sequence-dependent melting properties and electrophoretic migration of DNA in solution. Erlich, ed., *PCR Technology, Principles and Applications for DNA Amplification*, (W.H. Freeman and Co, New York, 1992), Chapter 7.

6. Single-Strand Conformation Polymorphism Analysis

Alleles of target sequences can be differentiated using single-strand conformation polymorphism analysis, which identifies base differences by alteration in electrophoretic migration of single stranded PCR products, as described in Orita *et al.*, *Proc. Nat. Acad. Sci.* 86, 2766-2770 (1989). Amplified PCR products can be generated as described above, and heated or otherwise denatured, to form single stranded amplification products. Single-stranded nucleic acids may refold or form secondary structures which

are partially dependent on the base sequence. The different electrophoretic mobilities of single-stranded amplification products can be related to base-sequence differences between alleles of target sequences.

7. Single Base Extension

- 5 An alternative method for identifying and analyzing polymorphisms is based on single-base extension (SBE) of a fluorescently-labeled primer coupled with fluorescence resonance energy transfer (FRET) between the label of the added base and the label of the primer. Typically, the method, such as that described by Chen *et al.*, (*PNAS* 94:10756-61 (1997), incorporated herein by reference) uses a locus-specific
- 10 oligonucleotide primer labeled on the 5' terminus with 5-carboxyfluorescein (FAM). This labeled primer is designed so that the 3' end is immediately adjacent to the polymorphic site of interest. The labeled primer is hybridized to the locus, and single base extension of the labeled primer is performed with fluorescently labeled
- 15 dideoxynucleotides (ddNTPs) in dye-terminator sequencing fashion, except that no deoxyribonucleotides are present. An increase in fluorescence of the added ddNTP in response to excitation at the wavelength of the labeled primer is used to infer the identity of the added nucleotide.

III. Methods of Use

- After determining polymorphic form(s) present in an individual at one or more
- 20 polymorphic sites, this information can be used in a number of methods.

A. Forensics

- Determination of which polymorphic forms occupy a set of polymorphic sites in an individual identifies a set of polymorphic forms that distinguishes the individual. *See generally* National Research Council, *The Evaluation of Forensic DNA Evidence* (Eds. Pollard *et al.*, National Academy Press, DC, 1996). The more sites that are analyzed,
- 25 the lower the probability that the set of polymorphic forms in one individual is the same

as that in an unrelated individual. Preferably, if multiple sites are analyzed, the sites are unlinked. Thus, polymorphisms of the invention are often used in conjunction with polymorphisms in distal genes. Preferred polymorphisms for use in forensics are biallelic because the population frequencies of two polymorphic forms can usually be
 5 determined with greater accuracy than those of multiple polymorphic forms at multi-allelic loci.

The capacity to identify a distinguishing or unique set of forensic markers in an individual is useful for forensic analysis. For example, one can determine whether a blood sample from a suspect matches a blood or other tissue sample from a crime scene
 10 by determining whether the set of polymorphic forms occupying selected polymorphic sites is the same in the suspect and the sample. If the set of polymorphic markers does not match between a suspect and a sample, it can be concluded (barring experimental error) that the suspect was not the source of the sample. If the set of markers does match, one can conclude that the DNA from the suspect is consistent with that found at
 15 the crime scene. If frequencies of the polymorphic forms at the loci tested have been determined (e.g., by analysis of a suitable population of individuals), one can perform a statistical analysis to determine the probability that a match of suspect and crime scene sample would occur by chance.

$p(ID)$ is the probability that two random individuals have the same polymorphic or
 20 allelic form at a given polymorphic site. In biallelic loci, four genotypes are possible: AA, AB, BA, and BB. If alleles A and B occur in a haploid genome of the organism with frequencies x and y , the probability of each genotype in a diploid organism is (see WO 95/12607):

- Homozygote: $p(AA) = x^2$
- 25 Homozygote: $p(BB) = y^2 = (1-x)^2$
- Single Heterozygote: $p(AB) = p(BA) = xy = x(1-x)$
- Both Heterozygotes: $p(AB+BA) = 2xy = 2x(1-x)$

The probability of identity at one locus (i.e, the probability that two individuals, picked at random from a population will have identical polymorphic forms at a given locus) is given by the equation:

$$p(\text{ID}) = (x^2)^2 + (2xy)^2 + (y^2)^2.$$

- 5 These calculations can be extended for any number of polymorphic forms at a given locus. For example, the probability of identity $p(\text{ID})$ for a 3-allele system where the alleles have the frequencies in the population of x , y and z , respectively, is equal to the sum of the squares of the genotype frequencies:

$$p(\text{ID}) = x^4 + (2xy)^2 + (2yz)^2 + (2xz)^2 + y^4 + z^4$$

- 10 In a locus of n alleles, the appropriate binomial expansion is used to calculate $p(\text{ID})$ and $p(\text{exc})$.

The cumulative probability of identity ($\text{cum } p(\text{ID})$) for each of multiple unlinked loci is determined by multiplying the probabilities provided by each locus.

$$\text{cum } p(\text{ID}) = p(\text{ID}_1)p(\text{ID}_2)p(\text{ID}_3)\dots p(\text{ID}_n)$$

- 15 The cumulative probability of non-identity for n loci (i.e. the probability that two random individuals will be different at 1 or more loci) is given by the equation:

$$\text{cum } p(\text{nonID}) = 1 - \text{cum } p(\text{ID}).$$

- If several polymorphic loci are tested, the cumulative probability of non-identity for random individuals becomes very high (e.g., one billion to one). Such probabilities
20 can be taken into account together with other evidence in determining the guilt or innocence of the suspect.

B. Paternity Testing

- The object of paternity testing is usually to determine whether a male is the father of a child. In most cases, the mother of the child is known and thus, the mother's
25 contribution to the child's genotype can be traced. Paternity testing investigates whether the part of the child's genotype not attributable to the mother is consistent with that of

the putative father. Paternity testing can be performed by analyzing sets of polymorphisms in the putative father and the child.

If the set of polymorphisms in the child attributable to the father does not match the set of polymorphisms of the putative father, it can be concluded, barring
 5 experimental error, that the putative father is not the real father. If the set of polymorphisms in the child attributable to the father does match the set of polymorphisms of the putative father, a statistical calculation can be performed to determine the probability of coincidental match.

The probability of parentage exclusion (representing the probability that a random
 10 male will have a polymorphic form at a given polymorphic site that makes him incompatible as the father) is given by the equation (see WO 95/12607):

$$p(\text{exc}) = xy(1-xy)$$

where x and y are the population frequencies of alleles A and B of a biallelic polymorphic site.

15 (At a triallelic site $p(\text{exc}) = xy(1-xy) + yz(1-yz) + xz(1-xz) + 3xyz(1-xyz)$), where x, y and z are the respective population frequencies of alleles A, B and C).

The probability of non-exclusion is

$$p(\text{non-exc}) = 1 - p(\text{exc})$$

The cumulative probability of non-exclusion (representing the value obtained
 20 when n loci are used) is thus:

$$\text{cum } p(\text{non-exc}) = p(\text{non-exc1})p(\text{non-exc2})p(\text{non-exc3})... p(\text{non-excn})$$

The cumulative probability of exclusion for n loci (representing the probability that a random male will be excluded)

$$\text{cum } p(\text{exc}) = 1 - \text{cum } p(\text{non-exc}).$$

25 If several polymorphic loci are included in the analysis, the cumulative probability of exclusion of a random male is very high. This probability can be taken into account in assessing the liability of a putative father whose polymorphic marker set matches the child's polymorphic marker set attributable to his/her father.

C. Correlation of Polymorphisms with Phenotypic Traits

The polymorphisms of the invention may contribute to the phenotype of an organism in different ways. Some polymorphisms occur within a protein coding sequence and contribute to phenotype by affecting protein structure. The effect may be neutral, beneficial or detrimental, or both beneficial and detrimental, depending on the circumstances. For example, a heterozygous sickle cell mutation confers resistance to malaria, but a homozygous sickle cell mutation is usually lethal. Other polymorphisms occur in noncoding regions but may exert phenotypic effects indirectly via influence on replication, transcription, and translation. A single polymorphism may affect more than one phenotypic trait. Likewise, a single phenotypic trait may be affected by polymorphisms in different genes. Further, some polymorphisms predispose an individual to a distinct mutation that is causally related to a certain phenotype. For example, the polymorphisms identified herein and shown in Table 3 are present in the chromosomal loci which have been identified as described herein as conferring susceptibility to IBD such as CD and UC.

Correlation is performed for a population of individuals who have been tested for the presence or absence of a phenotypic trait of interest and for polymorphic markers sets. To perform such analysis, the presence or absence of a set of polymorphisms (i.e. a polymorphic set) is determined for a set of the individuals, some of whom exhibit a particular trait, and some of which exhibit lack of the trait. The alleles of each polymorphism of the set are then reviewed to determine whether the presence or absence of a particular allele is associated with the trait of interest. Correlation can be performed by standard statistical methods such as a κ -squared test and statistically significant correlations between polymorphic form(s) and phenotypic characteristics are noted. For example, it might be found that the presence of allele A1 at polymorphism A correlates with heart disease. As a further example, it might be found that the combined presence of allele A1 at polymorphism A and allele B1 at polymorphism B correlates with increased susceptibility to IBD (e.g., CD and UC).

Such correlations can be exploited in several ways. In the case of a strong correlation between a set of one or more polymorphic forms and a disease for which treatment is available, detection of the polymorphic form set in a human or animal patient may justify immediate administration of treatment, or at least the institution of regular monitoring of the patient. Detection of a polymorphic form correlated with serious disease in a couple contemplating a family may also be valuable to the couple in their reproductive decisions. For example, the female partner might elect to undergo *in vitro* fertilization to avoid the possibility of transmitting such a polymorphism from her husband to her offspring. In the case of a weaker, but still statistically significant correlation between a polymorphic set and human disease, immediate therapeutic intervention or monitoring may not be justified. Nevertheless, the patient can be motivated to begin simple life-style changes (e.g., diet, exercise) that can be accomplished at little cost to the patient but confer potential benefits in reducing the risk of conditions to which the patient may have increased susceptibility by virtue of variant alleles. Identification of a polymorphic set in a patient correlated with enhanced receptiveness to one of several treatment regimes for a disease indicates that this treatment regime should be followed.

For animals and plants, correlations between characteristics and phenotype are useful for breeding for desired characteristics. For example, Beitz *et al.*, US 5,292,639 discuss use of bovine mitochondrial polymorphisms in a breeding program to improve milk production in cows. To evaluate the effect of mtDNA D-loop sequence polymorphism on milk production, each cow was assigned a value of 1 if variant or 0 if wildtype with respect to a prototypical mitochondrial DNA sequence at each of 17 locations considered. Each production trait was analyzed individually with the following animal model:

$$Y_{ijkpn} = \mu + YS_i + P_j + X_k + \beta_1 + \dots \beta_{17} + PE_n + a_n + e_p$$

where Y_{ijkpn} is the milk, fat, fat percentage, SNF, SNF percentage, energy concentration, or lactation energy record; μ is an overall mean; YS_i is the effect common to all cows calving in year-season; X_k is the effect common to cows in either the high or average

selection line; β_1 to β_{17} are the binomial regressions of production record on mtDNA D-loop sequence polymorphisms; PE_n is permanent environmental effect common to all records of cow n ; a_n is effect of animal n and is composed of the additive genetic contribution of sire and dam breeding values and a Mendelian sampling effect; and e_p is a random residual. It was found that eleven of seventeen polymorphisms tested

5 influenced at least one production trait. Bovines having the best polymorphic forms for milk production at these eleven loci are used as parents for breeding the next generation of the herd.

D. Genetic Mapping of Phenotypic Traits

10 The previous section concerns identifying correlations between phenotypic traits (e.g., IBD) and polymorphisms that directly or indirectly contribute to those traits, such as those identified in Table 3. The present section describes identification of a physical linkage between a genetic locus associated with a trait of interest and polymorphic markers that are not associated with the trait, but are in physical proximity with the

15 genetic locus responsible for the trait and co-segregate with it. Such analysis is useful for mapping a genetic locus associated with a phenotypic trait to a chromosomal position, and thereby cloning gene(s) responsible for the trait. See Lander *et al.*, *Proc. Natl. Acad. Sci. (USA)* 83, 7353-7357 (1986); Lander *et al.*, *Proc. Natl. Acad. Sci. (USA)* 84, 2363-2367 (1987); Donis-Keller *et al.*, *Cell* 51, 319-337 (1987); Lander *et al.*, *Genetics* 121, 185-199 (1989)). Genes localized by linkage can be cloned by a process known as directional cloning. See Wainwright, *Med. J. Australia* 159, 170-174 (1993); Collins, *Nature Genetics* 1, 3-6 (1992).

20

Linkage studies are typically performed on members of a family. Available members of the family are characterized for the presence or absence of a phenotypic

25 trait and for a set of polymorphic markers. The distribution of polymorphic markers in an informative meiosis is then analyzed to determine which polymorphic markers co-segregate with a phenotypic trait. See, e.g., Kerem *et al.*, *Science* 245, 1073-1080

(1989); Monaco *et al.*, *Nature* 316, 842 (1985); Yamoka *et al.*, *Neurology* 40, 222-226 (1990); Rossiter *et al.*, *FASEB Journal* 5, 21-27 (1991).

Linkage is analyzed by calculation of LOD (log of the odds) values. A lod value is the relative likelihood of obtaining observed segregation data for a marker and a
 5 genetic locus when the two are located at a recombination fraction θ , versus the situation in which the two are not linked, and thus segregating independently (Thompson & Thompson, *Genetics in Medicine* (5th ed, W.B. Saunders Company, Philadelphia, 1991); Strachan, "Mapping the human genome" in *The Human Genome* (BIOS Scientific Publishers Ltd, Oxford), Chapter 4). A series of likelihood ratios are
 10 calculated at various recombination fractions (θ), ranging from $\theta = 0.0$ (coincident loci) to $\theta = 0.50$ (unlinked). Thus, the likelihood at a given value of θ is: probability of data if loci linked at θ to probability of data if loci unlinked. The computed likelihoods are usually expressed as the \log_{10} of this ratio (i.e., a lod score). For example, a lod score of 3 indicates 1000:1 odds against an apparent observed linkage being a coincidence.
 15 The use of logarithms allows data collected from different families to be combined by simple addition. Computer programs are available for the calculation of lod scores for differing values of θ (e.g., LIPED, MLINK (Lathrop, *Proc. Nat. Acad. Sci. (USA)* 81, 3443-3446 (1984)). For any particular lod score, a recombination fraction may be determined from mathematical tables. See Smith *et al.*, *Mathematical tables for*
 20 *research workers in human genetics* (Churchill, London, 1961); Smith, *Ann. Hum. Genet.* 32, 127-150 (1968). The value of θ at which the lod score is the highest is considered to be the best estimate of the recombination fraction.

Positive lod score values suggest that the two loci are linked, whereas negative values suggest that linkage is less likely (at that value of θ) than the possibility that the
 25 two loci are unlinked. By convention, a combined lod score of +3 or greater (equivalent to greater than 1000:1 odds in favor of linkage) is considered definitive evidence that two loci are linked. Similarly, by convention, a negative lod score of -2 or less is taken as definitive evidence against linkage of the two loci being compared. Negative linkage

data are useful in excluding a chromosome or a segment thereof from consideration. The search focuses on the remaining non-excluded chromosomal locations.

IV. Modified Polypeptides and Gene Sequences

The invention further provides variant forms of nucleic acids and corresponding
 5 proteins. The nucleic acids comprise one of the sequences described in Table 3, in which the polymorphic position is occupied by one of the alternative bases for that position. Some nucleic acids encode full-length variant forms of proteins. Similarly, variant proteins have the prototypical amino acid sequences encoded by nucleic acid sequences shown in Table 3, (read so as to be in-frame with the full-length coding
 10 sequence of which it is a component) except at an amino acid encoded by a codon including one of the polymorphic positions shown in Table 3. That position is occupied by the amino acid coded by the corresponding codon in any of the alternative forms shown in Table 3.

Variant genes can be expressed in an expression vector in which a variant gene is
 15 operably linked to a native or other promoter. Usually, the promoter is a eukaryotic promoter for expression in a mammalian cell. The transcription regulation sequences typically include a heterologous promoter and optionally an enhancer which is recognized by the host. The selection of an appropriate promoter, for example trp, lac, phage promoters, glycolytic enzyme promoters and tRNA promoters, depends on the
 20 host selected. Commercially available expression vectors can be used. Vectors can include host-recognized replication systems, amplifiable genes, selectable markers, host sequences useful for insertion into the host genome, and the like.

The means of introducing the expression construct into a host cell varies depending upon the particular construction and the target host. Suitable means include
 25 fusion, conjugation, transfection, transduction, electroporation or injection, as described in Sambrook, *supra*. A wide variety of host cells can be employed for expression of the variant gene, both prokaryotic and eukaryotic. Suitable host cells include bacteria such as *E. coli*, yeast, filamentous fungi, insect cells, mammalian cells, typically

immortalized, *e.g.*, mouse, CHO, human and monkey cell lines and derivatives thereof. Preferred host cells are able to process the variant gene product to produce an appropriate mature polypeptide. Processing includes glycosylation, ubiquitination, disulfide bond formation, general post-translational modification, and the like. As used
5 herein, "gene product" includes mRNA, peptide and protein products.

The protein may be isolated by conventional means of protein biochemistry and purification to obtain a substantially pure product, *i.e.*, 80, 95 or 99% free of cell component contaminants, as described in Jacoby, *Methods in Enzymology* Volume 104, Academic Press, New York (1984); Scopes, *Protein Purification, Principles and*
10 *Practice*, 2nd Edition, Springer-Verlag, New York (1987); and Deutscher (ed), *Guide to Protein Purification, Methods in Enzymology*, Vol. 182 (1990). If the protein is secreted, it can be isolated from the supernatant in which the host cell is grown. If not secreted, the protein can be isolated from a lysate of the host cells.

The invention further provides transgenic nonhuman animals capable of
15 expressing an exogenous variant gene and/or having one or both alleles of an endogenous variant gene inactivated. Expression of an exogenous variant gene is usually achieved by operably linking the gene to a promoter and optionally an enhancer, and microinjecting the construct into a zygote. *See* Hogan *et al.*, "Manipulating the Mouse Embryo, A Laboratory Manual," Cold Spring Harbor Laboratory. Inactivation
20 of endogenous variant genes can be achieved by forming a transgene in which a cloned variant gene is inactivated by insertion of a positive selection marker. *See* Capecchi, *Science* 244, 1288-1292 (1989). The transgene is then introduced into an embryonic stem cell, where it undergoes homologous recombination with an endogenous variant gene. Mice and other rodents are preferred animals. Such animals provide useful drug
25 screening systems.

In addition to substantially full-length polypeptides expressed by variant genes, the present invention includes biologically active fragments of the polypeptides, or analogs thereof, including organic molecules which simulate the interactions of the peptides. Biologically active fragments include any portion of the full-length

polypeptide which confers a biological function on the variant gene product, including ligand binding, and antibody binding. Ligand binding includes binding by nucleic acids, proteins or polypeptides, small biologically active molecules, or large cellular structures.

- Polyclonal and/or monoclonal antibodies that specifically bind to variant gene
- 5 products but not to corresponding prototypical gene products are also provided. Antibodies can be made by injecting mice or other animals with the variant gene product or synthetic peptide fragments thereof. Monoclonal antibodies are screened as are described, for example, in Harlow & Lane, *Antibodies, A Laboratory Manual*, Cold Spring Harbor Press, New York (1988); Goding, *Monoclonal antibodies, Principles and*
- 10 *Practice* (2d ed.) Academic Press, New York (1986). Monoclonal antibodies are tested for specific immunoreactivity with a variant gene product and lack of immunoreactivity to the corresponding prototypical gene product. These antibodies are useful in diagnostic assays for detection of the variant form, or as an active ingredient in a pharmaceutical composition.

15 V. Kits

- The invention further provides kits comprising at least one allele-specific oligonucleotide as described herein. Often, the kits contain one or more pairs of allele-specific oligonucleotides hybridizing to different forms of a polymorphism. In some kits, the allele-specific oligonucleotides are provided immobilized to a substrate. For
- 20 example, the same substrate can comprise allele-specific oligonucleotide probes for detecting at least 10, 100 or all of the polymorphisms shown in Table 3. Optional additional components of the kit include, for example, restriction enzymes, reverse-transcriptase or polymerase, the substrate nucleoside triphosphates, means used to label (for example, an avidin-enzyme conjugate and enzyme substrate and chromogen if the
- 25 label is biotin), and the appropriate buffers for reverse transcription, PCR, or hybridization reactions. Usually, the kit also contains instructions for carrying out the methods.

The following Examples are offered for the purpose of illustrating the present invention and are not to be construed to limit the scope of this invention. The teachings of all references cited herein are hereby incorporated herein by reference.

EXAMPLES

5 With the goal of identifying IBD susceptibility genes, a genomewide scan was undertaken in 163 pedigrees, and three regions of suggestive linkage (3, 5q31-33, 6p) and one of significant linkage to 19p13 (LOD = 4.6) were identified. Higher density mapping in the suggestive 5q31-33 region revealed a CD susceptibility locus of genome-wide significance (LOD = 3.9). Importantly, the 5q31-p33 localizes to the
10 major immunoregulatory cytokine gene cluster and the 19p13 locus to a region containing numerous genes encoding cytokine/chemokine receptors and other inflammatory-associated molecules that could have a direct role in disease susceptibility.

In order to pursue the evidence of linkage to chromosome 5, a systematic linkage
15 disequilibrium (LD) approach was adopted. The approach that was used in the first stage of LD mapping was to genotype all known microsatellite markers in the 18 cM between D5S1435 and D5S1480, as these two markers delimit a region of a 2 LOD drop on either side of the linkage peak centered at marker D5S2497. All alleles for each marker were examined for evidence of excess transmission from heterozygous parents
20 to CD child using the transmission disequilibrium test (TDT). Only alleles at two of the 57 markers had significant C^2 results ($p < 0.001$): IRF1p1 ($C^2 = 13.3$, $p = 0.0003$) and D5S1984 ($C^2 = 14.0$, $p = 0.0002$) (Table 1). A second stage of mapping was then undertaken to confirm, as well as to better delimit, the region of LD surrounding IRF1p1 and D5S1984. The development of new microsatellite markers was necessary.
25 The marker with the most significant C^2 result was CAh17a ($C^2 = 16.2$, $p = 0.00006$) and was located between IRF1p1 and D5S1984 (Table 2). Furthermore, the alleles 193, 156, 373, 140, 222, and 307 at markers GAh18a, IRF1p, CAh15a, CAh17a, D5S1984, CSF2p10, respectively, define a haplotype conferring susceptibility to Crohn's disease

(CD). In order to identify the sequence variant that would explain the genetic susceptibility to CD provided by this haplotype, a search was performed for all single nucleotide polymorphisms (SNPs) in this region of LD. The SNP discovery was accomplished by direct sequencing of overlapping PCR products amplified from DNA samples from eight individuals (six CD patients, one unaffected family member, and one CEPH DNA as control). Table 3 shows the results of the SNP discovery analyses.

139 triads were genotyped for a total of 241 SNPs thus far, where at least 50 trios were fully genotyped. Using a C^2 value of 13 (corresponding to a p-value of 0.05) as threshold, 12 SNPs were found to have a significant level of association with CD and extended over a region of 250 kb, from IRF1 to prolyl4 hydroxylase. These were markers IGR2055a_1, IGR2060a_1, IGR2063b_1, IGR2069a_2, IGR2078a_1, IGR2096a_1, IGR2198a_1, IGR2230a_1, IGR2277a_1, IGR3081a_1, IGR3096a_1, PROLYLex3_1 (see Table 4). Any of these best SNPs by themselves are in strong association with CD and fully explain the microsatellite LD observations. Furthermore, the best SNPs have nearly identical association characteristics (that is, the allele at one SNP determines the allele of all others on any phased chromosome), confirming that a single risk haplotype extending approximately 250 kb is the source of all the observations of association in this region. Specifically, this haplotype is defined by the alleles G, C, G, T, A, A, G, T, G, G, C, T at markers IGR2055a_1, IGR2060a_1, IGR2063b_1, IGR2069a_2, IGR2078a_1, IGR2096a_1, IGR2198a_1, IGR2230a_1, IGR2277a_1, IGR3081a_1, IGR3096a_1, PROLYLex3_1, respectively. The frequency of this haplotype is estimated to be approximately 37% in the general population. Furthermore, this haplotype is transmitted from heterozygous parents to CD patients at a ratio of 2.5:1.

25 Families

For the linkage study, multicase families with 2 or more siblings affected by IBD were identified by review of clinical charts of all patients registered in the Mount Sinai

Hospital Inflammatory Bowel Disease Unit patient database and from the Hospital for Sick Children IBD database. Patients were also referred by physicians in the Greater Toronto Area (GTA). To confirm and update information obtained from these records, all patients were sent a questionnaire inquiring about the presence of a family history of IBD. Individuals identified as having other affected first-degree relatives were invited to participate and asked for permission to contact other affected and unaffected family members. Endoscopic, histological and radiological reports as well as clinical data were obtained on all affected individuals and these reports were reviewed for verification of diagnosis based upon standard criteria. Venous blood sampling was performed on affected individuals and their parents, and DNA was extracted using a salting out procedure. Ethics approval for this study was given by the University of Toronto Ethics Committee and written informed consent was obtained from all participants.

All of the LD analyses in this study were performed with father-mother-affected child (CD only) triads, where 0 or 1 of the parents was affected with CD. These triads either came from the multicase families used in the linkage stage of this study or were identified specifically for the purpose of the LD study. Specifically, for the microsatellite genotyping, 296 triads were genotyped: 95 of these triads were derived from families used in the original identification of the IBD5 locus (only one triad per family), and 201 were from newly collected families. For the SNP genotyping, 139 triads were genotyped: 18 were derived from families used in the original identification of the IBD5 locus, and 121 were from the newly collected families. Individuals affected by CD were identified by review of the clinical charts of all patients registered in the Mount Sinai Hospital Inflammatory Bowel Disease Centre patient database and from the Toronto Hospital for Sick Children IBD database. Written informed consent was obtained from all participants and ethics approval for this study was granted by the University of Toronto Ethics Committee.

Microsatellite Genotyping

Genomic DNA was extracted from peripheral blood lymphocytes from probands and family members from 163 Caucasian pedigrees. The genome-wide scan, with an average inter-marker spacing of 12 cM, was carried out using a modified version of the
5 Cooperative Human Linkage Centre (CHLC) Screening Set/version 6.0 that also included Genethon markers. These 312 loci were amplified using fluorescently-labeled primers (Research Genetics Inc., Huntsville AL) in separate polymerase chain reactions, and the products were then multiplexed into panels by pooling before electrophoresis on ABI 377 sequencers (PE Applied Biosystems,
10 Foster City, CA). Fluorescent genotyping gels were analyzed in an automated system developed at the Whitehead Institute/MIT Center for Genome Research. Further details of the genotyping system have previously been described (Rioux *et al.*, *Gastroenterology* 115:1062-1065 (1998)).

The region of suggestive linkage on chromosome 5 and the surrounding regions of
15 poor information content were followed up with 34 additional microsatellite markers. Specifically, 34 markers were genotyped between markers D5S1470 and D5S1471, decreasing the average spacing between markers to approximately 3 cM in this 125 cM region. This higher density mapping was performed on the original samples and on additional 12 families, for a total of 175
20 pedigrees analyzed. These new families consisted of 16 CD affected sibpairs.

In the first phase of the microsatellite LD mapping, a total of 57 microsatellite markers were genotyped on 296 CD triads. Information regarding primer sequence, allele size range, and suggested amplification conditions for 55 of these genetic markers (all but IRF1p1 and CSF2p10) can be obtained from the Genethon
25 (<http://www.genethon.fr/>), Marshfield (<http://research.marshfieldclinic.org/genetics/>), or Genome Database (<http://www.genethon.fr>) World Wide Web sites. The markers IRF1p1, CSF2p1, and the 8 markers used in the 2nd stage of LD mapping, were designed during the course of this study. Genotypes for all of these markers were obtained as described above.

SNP Discovery

In order to identify all SNPs in the *IBD5* critical region, a tiling path of overlapping PCR products was designed. Specifically, PCR assays were designed using Primer 3.0 to be approximately 700 bp in length, with 100 bp overlap with adjacent
5 assays. The -21 M13 forward and the -28 M13 reverse sequences were added to each of the forward and reverse PCR primers, respectively. These PCR primers were used to amplify 50 ng of genomic DNA from six CD patients, one unaffected family member, and one CEPH DNA as control. The PCR products were purified using the solid phase reversible immobilization (SPRI) method and then sequenced using the appropriate -21
10 M13 or -28 M13 DYEnamic Direct Cycle Sequencing kit (Amersham Pharmacia Biotech Ltd, Cleveland, OH). All sequencing reactions were run on ABI377 automated sequencers (PE Applied BioSystems, Foster City, CA); the gel files were processed using the BASS software, available on the Whitehead Institute/MIT Center for Genome Research FTP site. Sequences were base-called by the Phred program, and then the
15 forward and reverse reads were assembled by the Phrap program. All traces were visually inspected by at least two observers.

SNP genotyping

SNP genotyping was performed using length-multiplexed single-base extension (LM-SBE) as previously described. Briefly, PCR primers were designed as close as
20 possible to the SNPs identified in the current study, resulting in a product of a maximum length of 150 bp. Forward primers had T7 tails at their 5' ends and reverse primers had T3 tails at their 5' ends. These T7 and T3 tails were used for secondary amplification. Primer pairs were checked for homology to all amplicons and sorted into pools consisting of up to 50 primer pairs. Loci were subjected to two rounds of PCR
25 amplification. In the first round, 10 ng of genomic DNA was amplified using a pool of primer pairs (0.1 mM) and 2.5 units of Amplitaq Gold (Perkin Elmer). In the second round, a 3 mL aliquot of the primary amplification product was amplified with biotinylated-T7 and biotinylated-T3 primers. A 7 mL aliquot of this secondary

amplification product was purified from the unincorporated dNTPs using streptavidin-coated Dynabeads (Dyna). A multiplex SBE reaction was then carried out on the purified product using SNP-specific primers, JOE-ddATP (0.12 M), TAMRA-ddCTP (0.12 M), FAM-ddGTP (0.12 M), ROX-ddUTP (0.60 M; NEN DuPont) and

- 5 Thermosequenase (0.5 U; Amersham). Excess ddNTPs were removed from the SBE products using 96-well gel filtration blocks (Edge Biosystems) prior to electrophoresis on ABI 377 sequencers. The SBE gels were analyzed using a system developed at the Whitehead Institute/MIT Center for Genome Research as previously described.

Statistical analysis

- 10 Nonparametric multipoint linkage analysis of the data from the genome-wide scan and the higher density mapping on chromosome 5 was performed using the MAPMAKER/SIBS functions implemented in GENHUNTER 2.0. It is important to note that all sib pairs from sibships with more than 2 affecteds were counted but were conservatively downweighted by a factor of $2/n$ (where n = the number of affecteds).
- 15 Exclusion mapping was also performed with this software package, and a locus $8s > 2$ was considered excluded at a LOD score of -2.

- To establish appropriate thresholds for suggestive and significant genome-wide linkage for these particular datasets, simulations were performed by generating artificial genotype data with the identical family structures. These simulations matched the
- 20 datasets with respect to marker density, marker informativeness, the individuals genotyped, affected status, and the fraction of missing data.

- To assess the significance of the TDT results for each marker, permutation tests using the same genotype data were carried out. For each trio, chromosomes were randomly reassigned as transmitted or untransmitted to form a permuted dataset. The
- 25 number of permuted datasets with values as significant as that seen for the best single-marker and two-marker tests were tabulated. In order to quantify the extent of LD in the *IBD5* region, 3-marker haplotypes were examined using the TDT and P_{excess}
- (d). P_{excess} represents the strength of LD and is calculated by $(p_{\text{affected}} - p_{\text{normal}}) / (1$

[illegible]

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any other person who is not a member of the family of the person who is the subject of the investigation.

[illegible]

Table 1. Summary of the first stage of LD mapping using microsatellite markers.

Marker #	Marker Name	Source of marker ¹	Estimated Genetic Position ²	Distance to next marker	Previous linkage results (MLOD) ³	Allele	TDT results ⁴	pvalue
5	1 D5S1435	G	128.50	0.50	0.76	115	5.84	0.016
	2 AFMa113ye9	G	129.00	0.83		-	-	-
	3 D5S1505	M	129.83	0.00	0.79	-	-	-
	4 D5S1384	U	129.83	0.00		-	-	-
	5 D5S471	G	129.83	0.57	0.79	238	7.58	0.0059
10	6 D5S632	G	130.40	0.20		114	4.59	0.032
	7 D5S818	M	130.60	0.20		-	-	-
	8 D5S2502	M	130.80	0.10		-	-	-
	9 AFMB352XH5	G	130.90	0.04		-	-	-
15	10 D5S1975	G	130.94	0.00		-	-	-
	11 D5S622	G	130.94	1.86		-	-	-
	12 D5S2059	G	132.80	0.85		190	5.83	0.016
	13 D5S615	U	133.65	0.00	1.8	-	-	-
	14 D5S804	M	133.65	0.00	1.8	-	-	-
	15 D5S1495	M	133.65	0.00	1.8	382	4.00	0.045
20	16 GATA68A03	M	133.65	0.35	2.2	-	-	-
	17 D5S809	M	134.00	0.40	2.1	-	-	-
	18 D5S2120	G	134.40	0.20		-	-	-
	19 D5S642	G	134.60	0.65	2.6	-	-	-
	20 D5S2057	G	135.25	0.00	3.1	-	-	-
25	21 D5S2110	G	135.25	0.62	3.1	-	-	-
	22 IRF1p1	S	135.87	0.19		156	13.27	0.00027
	23 D5S1984	G	136.06	0.16		222	14.04	0.00018
	24 CSF2p10	S	136.22	0.58		307	4.00	0.045
	25 D5S2497	G	136.80	0.10	3.9	129	7.69	0.0055
30	26 w2429/240wa7	G	136.90	0.10		-	-	-
	27 w866/057vg5	G	137.00	0.10		-	-	-
	28 D5S1766	U	137.10	0.10	3.5	245	6.48	0.011
	29 D5S808	M	137.20	0.10	3.3	-	-	-
	30 D5S458	G	137.30	0.00	3.1	-	-	-
35	31 D5S396	G	137.30	0.09		-	-	-
	32 D5S2053	G	137.39	0.56	3.0	-	-	-
	33 D5S1995	G	137.95	0.69	2.8	-	-	-
	34 D5S2115	G	138.64	0.68	2.4	-	-	-
	35 IL9	M	139.32	0.01	2.0	-	-	-
40	36 D5S816	M	139.33	0.07	2.0	-	-	-
	37 D5S393	G	139.40	0.10	2.0	-	-	-
	38 D5S399	G	139.50	0.90	2.0	127	4.57	0.032
	39 D5S479	G	140.40	0.10		-	-	-
	40 AFM350yb1	G	140.50	0.10		-	-	-
45	41 D5S1983	G	140.60	0.12		116	4.55	0.033
	42 D5S476	G	140.72	0.00	1.7	-	-	-
	43 D5S500	G	140.72	0.28	1.7	211	4.15	0.042
	44 AFMB290YC9	G	141.00	0.82		-	-	-
	45 D5S414	G	141.82	0.98		-	-	-

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46	D5S2009	G	142.80	0.12		140	6.70	0.01
47	D5S658	G	142.92	0.00	2.0	-	-	-
48	D5S2116	G	142.92	1.08		-	-	-
49	D5S2011	G	144.00	0.06		-	-	-
50	D5S2119	G	144.06	0.00		-	-	-
51	D5S1979	G	144.06	1.15		-	-	-
52	D5S2017	G	145.21	2.19	2.2	91	5.40	0.02
53	D5S2859	M	147.40	0.09		-	-	-
54	D5S436	G	147.49	0.00	1.6	-	-	-
55	D5S207	M	147.49	0.00		-	-	-
56	D5S1480	M	147.49		1.6	-	-	-

¹ Abbreviations: G, Genethon; M, Marshfield; U, Utah; S, designed by authors from genomic sequence.

² Estimated from genetic (Genethon, Marshfield) and physical (data not shown) map information

³ Linkage data for the CD subgroup with early onset disease as seen in figure 1 and reference ###

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⁴ Results are shown only if pvalue < 0.05

Table 2. Summary of combined LD mapping information.

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Marker #	Marker Name	Distance to next marker (kb)	LD mapping stage	Allele	T:U	results X ²	pvalue
57	CAh14b	43	2	-		-	-
58	ATTh14c	167	2	-		-	-
59	IL4m2	164	2	214	1.8	4.74	0.029
60	GAh18a	21	2	193	1.4		0.018
22	IRF1p1	24	1	156	1.7	13.27	0.00027
61	CAh15a	130	2	373	1.5	7.73	0.0054
62	CAh17a	97	2	140	1.8	16.19	0.00005
						7	
23	D5S1984	163	1	222	1.8	14.04	0.00018
24	CSF2p10	178	1	307	1.4	4.00	0.045
63	CAh81b	85	2	-		-	-
64	CAh81c		2	-		-	-

TABLE 3
 Genomic regions associated with the expression of the gene, including the 5' and 3' UTRs, and the flanking regions.

Legend:	EST:	expressed sequence tag	known gene	gene:
Predicted gene:	ins/del:	insertion/deletion	gene predicted from genomic sequence using the GENSCAN package	
genomic:	derived from resequencing of entire genomic region (therefore includes genes, promoters, enhancers, etc.)			
Notes:	1) "N" in sequence represents polymorphic base			
	2) details are provided where currently available			
	3) This list includes all polymorphisms: SNPs, repeats, and insertions/deletions			
Polymorphism	Poly type	comment #1 Polymorphism details	comment #2 Verification	comment #3
Name		Status	Position on reference genomic sequence (attached)	Gene Name
				Flanking Sequence
1 CSF2_6610	c/t	Verified	gene	n/a
2 CSFenh_1492	g/t	Verified	gene	n/a
3 CSFenh_1580	g/t	Verified	gene	n/a
4 CSFex4_6632	c/t	Verified	gene	n/a
5 E4ex1_1	t/c	Verified	EST	n/a
6 E4ex1_2	a/g	Verified	EST	n/a
7 E4ex1_3	t/c	Verified	EST	n/a
8 Facoex16_1	g/c	Verified	gene	n/a
				Fatty acid CoA ligase
				aaactctctgtgcaaccacagaNtatcacctttgaaa gtttcaag
				attctctccctgtgataatgtctctcgtNataagga tcttgagtgactcaagc
				acacgcataggaacactccttccagagggttttcNc ctgtctctgtaggaaggggggcccagagg
				aaaggaaactctctgtgcaaccacagaNtatcacct ttgaaagttcaagaga
				ctgggaaccccaaacatctctggagaaNagcigag aacctaccaaggga
				agacagaaaattagcttagagatggagggtggca Ngatctctaaagctgtctcccgctgcc
				atgggagggtggcac-
				gatctctaaagctgtccNgcgtccattcaggagtgc ctcatgcataag
				ggctactgtgaaagatccagacaggaNgaaggag gcccggacagcgatggc

GenBank accession numbers are provided for the sequences of the genes. The sequences are available in GenBank under the accession numbers listed in the table.

9	FaCoex1_1	t/c	Verified	gene	n/a	Fatty acid CoA ligase	accaggaggccctgtgctaccactgctaaNggctct accaccacccggctctc
10	GENS010ex2_1	t/c	Verified	Predicted gene	n/a		agaagcagtagggcNactactaggtagcccca
11	GENS020ex1_1	a/g	Verified	Predicted gene	n/a		gggtgtgacagaggcgtNtggcaggactc
12	GENS020ex3_1	a/c	Verified	Predicted gene	n/a		ggcgccacNcaaacctctgctgcagctc
13	GENS020ex3_2	t/g	Verified	Predicted gene	n/a		aggccagccctNtcttactatgtcct
14	GENS020ex3_3	a/g	Verified	Predicted gene	n/a		tagaagcagaagggtgtggtggccctcNctggtgtg ggacttctgcccactgcac
15	GENS021ex1_1	g/c	Verified	Predicted gene	n/a		tcatggcgggtgtgtgacctgagagaggNtca gatgaagaagcctgggtgaggaatgag
16	GENS021ex1_2	t/c	Verified	Predicted gene	n/a		aaggccctcatgattcatgattNgtggtttgtgtg tccatgcct
17	GENS025ex1_1	a/g	Verified	Predicted gene	n/a		gctcaagccctggggagggaaggagggtgctg acccac
18	GENS026ex12_1	a/t	Verified	Predicted gene	n/a		cttcatgtagaagagcgtagtagtactgtattNtata atgttaccatgtccatataaacaagctcc
19	GENS026ex3_1	t/c	Verified	Predicted gene	n/a		tcttctcacaaactcctaagtagtaccNtagagca ataggactcctgtataa
20	GENS026ex4_1	t/c	Verified	Predicted gene	n/a		gggtttgtgtatctaaataggNgacctcagcctta aaacctcatct
21	GENS026ex5_1	t/c	Verified	Predicted gene	n/a		tggaaaaatcaattaccctgtattacNtgtgtgga gaaatgaaggcatt
22	GENS026ex5_2	a/g	Verified	Predicted gene	n/a		cagtaaatatytaggcctatgtc
23	GENS026ex6_1	t/g	Verified	Predicted gene	n/a		aatttattttgtcttttaataagtaNctct- ctgctcatttggtatctgctatctcgtg
24	GENS026ex6_2	t/c	Verified	Predicted gene	n/a		tatttattgtcttttaataagta- ctctNctgtcatttggtatctgctatctcgtg
25	GENS027ex2_1	a/g	Verified	Predicted gene	n/a		gcaatgctgtttttcttttagtatacaaaaNtgaatcctt cttccctcaaaagcttga
26	GENS027pro_1	a/c	Verified	Predicted gene	n/a		ccccaccatctctcggtggcggaagggaNaatg gtatctttaataccaaaaagataat

27	GENS027pro_2	t/c		Verified	Predicted gene	n/a	atctttgaggctttatgaaccacacatatggtNgaaaa cattgtggcctctggcacaga
28	GENS02ex2_1	a/g		Verified	Predicted gene	n/a	ccalctatgtaggtaacNgaggcaaaagcaaggg ctagggaga
29	GENS02ex3_1	g/c		Verified	Predicted gene	n/a	gggaggcgagacattaggcaaaataatNacatggat ctctgaaaaacatagctctctacga
30	GENS02ex4_1	t/g		Verified	Predicted gene	n/a	agaggaatgggggtggagttggcagNggggctggt tctcggctctccccga
31	GENS030ex2_1	a/g		Verified	Predicted gene	n/a	ctggcttagggccaagaactggccaNgttacagtt ccacacagataccg
32	GENS030ex3_1	a/t		Verified	Predicted gene	n/a	agggtagtgagggtgtactagggaNctggacact gagccccgaagttgggg
33	GENS030ex4_1	a/g		Verified	Predicted gene	n/a	gcggctgcagggggaggcacaagcNltgggccca ggcgccaagcgcc
34	GENS030pro_1	t/c		Verified	Predicted gene	n/a	atgtgtaccatggcccaactaatgtttga
35	GENS031ex1_1	t/c		Verified	Predicted gene	n/a	ctgggtaaaacacaggctgccctggacaaaagcNgg aaacagaaatgaggctccaggcggtgatt
36	GENS031pro_1	a/t		Verified	Predicted gene	n/a	ccacattttctaataccagtcatactatgNtggacattt gggttggtccaagctctttgc
37	GENS036ex1_1	t/g		Verified	Predicted gene	n/a	tccttcacaggacaggaattctgcaaaaNaaacat ttcattagcttgcattggtaagcat
38	GENS036ex1_2	t/c		Verified	Predicted gene	n/a	aaatgggtactgtataccattaccctatctgctttNggg gtgggtggcgggggggga
39	GENS037ex1_1	a/g		Verified	Predicted gene	n/a	aatagggtgcgatttgcagtgacaatgtgagNcaat tagttatcaggagaaagctaacgatg
40	GENS037pro_1	a/c		Verified	Predicted gene	n/a	tgaacttagctctcttggtaaataggaaaatNgctc caactactgtccaccccaagaaac
41	GENS038ex3_1	a/c		Verified	Predicted gene	n/a	tatctgcgcctctccctccacagcttgcagNcttc atctaattgaaaaagccagatgctcg
42	GENS038pro_1	t/c		Verified	Predicted gene	n/a	tccccccctgtttcgtcccgatctctgttcNcatctt atctcatggggaggaattctccaacct
43	GENS039ex4_1	a/g		Verified	Predicted gene	n/a	ctcttgtcaacatatatttaattaaatacNaggaaa aacaataaataactcgttggctga
44	GENS039ex7_1	a/g		Verified	Predicted gene	n/a	atgtgccttttctgtctctctccctcNtttctctagaagt cctccagaaacc

					Verified	Predicted gene	n/a			
45	GENS039ex7_2	t/g			Verified	Predicted gene	n/a			ctgagtgccgctacttggccgtgtgacccccNctac ggccctgtttcctaattctgtga
46	GENS03ex2_1	a/g			Verified	Predicted gene	n/a			ataatgcagaaacaaattagagaaaaactccNgIc aggctctccactcaccatggctgtgtggct
47	GENS03ex6_1	a/g			Verified	Predicted gene	n/a			aaacaaacaatgcccgccagagtcaccNgggct ggccatttgaaaagagtacatcag
48	GENS03ex6_2	a/t			Verified	Predicted gene	n/a			gggaggggctcttggaaacccagagagaccNgtag gaggggactgccggcaggagcgttg
49	GENS043ex1_1	a/g			Verified	Predicted gene	n/a			gcggcatctccatctctccaatgaacttgagcNrga gcaatgaacttgagtgtacagtcctcat
50	GENS043ex2_1	a/c			Verified	Predicted gene	n/a			tacttatctcaatcgcagttggtgaaaaaNicig caaatacgtagccctcccagttcaa
51	GENS044ex1_1	t/c			Verified	Predicted gene	n/a			cagtagtctaggaaagagaigtggattactgcNt cigtgcaatgataaagcagtaagttatccg
52	GENS044ex2_1	t/c			Verified	Predicted gene	n/a			tgtagtaaaaaacattcaaaaatcctctctcNagctat caagtattttgtaatttg
53	GENS044ex2_2	t/g			Verified	Predicted gene	n/a			ctaaaciggggtcatatttccatcagccNcattct gctaatgccagaigccctgggaag
54	GENS044ex2_3	a/c			Verified	Predicted gene	n/a			tctgctaagtccagatgccctgggaagNtcttcact gccatcttgggaaggatgcaga
55	GENS044ex2_4	t/c			Verified	Predicted gene	n/a			ccTgggaagatcttcacttgccatcNtggaaggatg cagaatgtgtgat
56	GENS044ex3_1	a/g			Verified	Predicted gene	n/a			ctgctcccatctccctataccatgtctgaNccctga gccataacatggatggacagc
57	GENS045ex10_1	g/c			Verified	Predicted gene	n/a			aagctacacaagaatgggcatttggccctttNaccaa catgtgtcttgactt
58	GENS045ex10_2	t/c			Verified	Predicted gene	n/a			cagcaaaaccccatgcataaacatcagcatftcaNg gctgaggccacacacagaaagccatcag
59	GENS045ex10_3	a/g			Verified	Predicted gene	n/a			aaaccccatgcaaacatcagcatftcacNgctga ggccacacacagaagcc
60	GENS045ex10_4	g/c			Verified	Predicted gene	n/a			ggtagcccaacagatgttctgtgtggtaccaacNga gaaaagcccatcttttaaacagc
61	GENS045ex10_5	t/c			Verified	Predicted gene	n/a			gccatcttttaaacagcagaaatctcactcgtcNc ctgtcccaactctctccctgtcaatccccaggac
62	GENS07ex1_1	t/c			Verified	Predicted gene	n/a			ccatctgagacctcatcagccacgccttcactttcca Natcaccatcagcatcttggttacaac

63	GENS09ex5_1	t/g		Verified	Predicted gene	n/a	gggcttgccgagcactgggcccNgggacgcaga cccaa
64	GENS09ex5_2	a/g		Verified	Predicted gene	n/a	cagcactgggcgggggacgcagacccaaNacg acagcaggcagcgcgagcg
65	GENS09pro_1	t/c		Verified	Predicted gene	n/a	tgaaggggccgacatggcaatgaatcta
66	IGR1000a_1	a/g		Verified	genomic	513	cccaggtgtgttNgaactcctggctt
67	IGR1002a_1	g/c		Verified	genomic	418	actctgggcccNgltgtgtggt
68	IGR1002a_2	t/c		Verified	genomic	422	gctgggcccgggtgNgtgtgtcacc
69	IGR1002a_3	g/c		Not yet verified	genomic	477	aggcagggtgatcacNaggicaagga
70	IGR1002a_4	other/w +	Poly t	Verified	genomic	259	gtaaaaatttaNttttttt
71	IGR1002a_5	a/t		Verified	genomic	405	ttagaaaaacNactgtctgggccc
72	IGR1003b_1	a/c		Verified	genomic	210	ctcagaaaaacaaaaaNaacaaaaaagaaac
73	IGR1003b_2	other/w +	Poly t	Verified	genomic	1	taaaaaatttaaNtttttttttt
74	IGR1004a_2	other/w +	Poly a	Verified	genomic	395	aaaaaNaacaacacatttagag
75	IGR1006a_1	t/g		Verified	genomic	389	aactcctgacctaangtgcgcgtgctt
76	IGR1006a_2	ins/del		Verified	genomic	169	gtttttttNtttgagacagaa
77	IGR1007a_1	t/c		Verified	genomic	190	tttcctttaccatNctgtcctcatat
78	IGR1007a_2	t/c		Verified	genomic	196	ccatcctgtcNcatatacaaaact
79	IGR1008a_1	other/w +	Poly t	Verified	genomic	605	tgggtgtcttctacNtttttttt
80	IGR1008a_2	t/c		Verified	genomic	385	tattttgtccctcNgtggattctct
81	IGR1009a_1	t/c		Verified	genomic	373	gtgcgggatttaNagggtgaaccac
82	IGR1009a_2	t/c		Verified	genomic	389	agggtgaaccacgtNcccagccacttc
83	IGR1010a_1	other/w +	ca repeat	Verified	genomic	186	ttcatttatgcacatNacacacacac
84	IGR1011a_1	g/c		Verified	genomic	207	ttccatccactgtNacagtgtattt
85	IGR1012a_1	t/g		Verified	genomic	520	ggaattctgcacaaaNaacatttcatta
86	IGR1012a_2	t/c		Verified	genomic	556	ggtgaagcattgtctNtgctgtcgtgt
87	IGR1013a_1	t/c		Verified	genomic	247	accattacatctgtcttNgggggtgggtggcgagg
88	IGR1015a_1	a/c	a in ref. sequence	Verified	genomic	202	tcctccttgagtgtctctcaNcggcttctgggttac

qPCR amplification was performed using the following primers and conditions. The reaction mixture (20 µl) contained 10 µl of the template DNA, 10 µl of the reaction mix, and 0.5 µl of the primer. The reaction was performed in a 96-well plate using a thermal cycler. The cycling conditions were 95°C for 30 s, 55°C for 30 s, and 72°C for 30 s. The reaction was repeated three times for each sample.

89	IGR1016a_1	a/g		Verified	genomic	300	cacgccaccatcNtcttagccttggttt
90	IGR1016a_2	ins/del		Verified	genomic	420	atctgtctcNatgctttcccc
91	IGR1016a_3	t/g		Verified	genomic	103	ccctacaaccNatctgtcag
92	IGR1017a_1	t/c		Verified	genomic	537	aagggtgtcagctccNaaggagtgttagaa
93	IGR1019a_1	t/c		Verified	genomic	366	gagcagcacatggNccaaagttagagctaag
94	IGR1020a_1	t/c		Verified	genomic	590	tcaccacagccagaggaactaNtctgttaatt
95	IGR1021a_1	t/g		Verified	genomic	237	gggtatttagaacaNgggattgagagctgc
96	IGR1021a_2	g/c		Verified	genomic	314	gcagatttttgNttctgtaaat
97	IGR1021a_3	t/c		Verified	genomic	411	agttcataatttaaNgtttttcagg
98	IGR1021a_4	ins/del	2 bp deletion	Verified	genomic	187	ctctttactctNtaccatataccat
99	IGR1022a_1	g/c		Verified	genomic	402	aaccctctaaagatatatttNaaaggactttctaaag gaa
100	IGR1022a_2	g/c		Verified	genomic	522	gtgcaaggccctaacgttttaNttgctctggtatcgca
101	IGR1022a_3	t/c		Verified	genomic	608	tcctgtctggctgNtgagtgctctgccag
102	IGR1023a_1	a/c		Verified	genomic	477	tttgtaaataggaaatNgtcccaactactgtc
103	IGR1025a_1	other/w +	ca repeat	Verified	genomic	557	ggagattttataNacacaca
104	IGR1026a_2	other/w +	Poly a	Verified	genomic	429	ccctatctcaNaaaaa
105	IGR1026a_3	ins/del		Verified	genomic	520	atgaaatgagatagtcagctaaanGccccgaag ag
106	IGR1027a_1	a/g		Verified	genomic	480	agagcaagctNaggagctc
107	IGR1027a_2	g/c	g on ref. sequence	Verified	genomic	497	gctctggacggcNagccccggaacc
108	IGR1029a_1	a/g		Verified	genomic	497	acaatgtgagNcaattagttt
109	IGR1030a_1	a/g		Verified	genomic	554	agcactggggNacaatgtt
110	IGR1031a_1	other/w +	Poly t	Verified	genomic	200	tcaggaatgacNttttttt
111	IGR1031a_3	a/c		Not yet verified	genomic	565	aagagctacNgtcttaccaa
112	IGR1032a_1	t/c		Verified	genomic	175	ccctaccccNagcaglgaa
113	IGR1032a_2	other/w +	Poly t	Verified	genomic	352	taatgaatttcNttttt
114	IGR1034a_1	a/g		Verified	genomic	293	tgaatggcNcagctcagct
115	IGR1039a_1	t/g		Verified	genomic	462	ccttggcacNtactcagcct

genomic data from the same region as the reference genome. The data was obtained from the same region as the reference genome. The data was obtained from the same region as the reference genome.

116	IGR1040a_1	t/c		Verified	genomic	188	ctggccagagNggccctcccc
117	IGR1040a_2	t/g		Verified	genomic	356	aggatttcaNgcaggaaagt
118	IGR1040a_3	a/c		Verified	genomic	633	agctgtcagNcttcatctaatt
119	IGR1043a_1	a/g	g in ref. sequence	Verified	genomic	170	ggatctgcacNggaaggaatt
120	IGR1043a_2	a/g		Verified	genomic	377	gtacttgttNattaaataat
121	IGR1045a_2	t/c		Verified	genomic	200	ttgacaaaaNiggccatga
122	IGR1045a_3	a/t		Verified	genomic	291	tagaagatttNaaaatgtaa
123	IGR1045a_4	t/c		Verified	genomic	99	cacagctcaNatccagccaccccaa
124	IGR1046a_1	t/g		Verified	genomic	301	gtgcatggNgtccccctccc
125	IGR1046a_2	t/c		Verified	genomic	337	tctcgttcNcatcttacc
126	IGR1046a_3	t/c		Verified	genomic	572	tccalactNgttgaatg
127	IGR1047a_1	ins/del		Verified	genomic	253	agagcacaNacacatgga
128	IGR1050a_1	a/g		Verified	genomic	235	ctagatgaagggcataNgcagaagacattt
129	IGR1050a_2	a/t		Verified	genomic	558	gggctgggttcocgNggcgcaagggg
130	IGR1052a_1	t/c		Verified	genomic	319	cctcgtaaatactcttNcagccttaaacct
131	IGR1055a_1	a/g		Verified	genomic	566	attaaatacNaggaaaaacaat
132	IGR1056a_2	t/g		Verified	genomic	235	tattaccagggaactcctggNgtccactgtcttag
133	IGR1056a_3	t/c	this base is missing on ref. seq.	Verified	genomic	285	aaccctggctccaagtgcNagcagccacagtctt c
134	IGR1057a_1	t/c	this base is missing on ref. seq.	Verified	genomic	271	ttcgaagttcagtgtaacNgtccctcgcgaaa
135	IGR1057a_2	a/g		Verified	genomic	390	gacaaagagggtcagcacNtgagtagaacgc
136	IGR1060a_1	g/c		Verified	genomic	279	aaggagcggactctactaaNgaatcctcctglaag g
137	IGR1060a_2	t/g		Verified	genomic	306	tgtaaagggcggccctatNatgggtctggggagaat
138	IGR1063a_2	a/g		Verified	genomic	425	tctcgtctctccctcNtttcttagaagctctcc
139	IGR1064a_1	t/g		Verified	genomic	335	tggccgtgtgaccccNctacgggctgttctcta
140	IGR1066b_1	a/g		Verified	genomic	90	taccaaagggccgcctccNggcacttggcgcagt g
141	IGR1068a_1	other/w +	poly T	Verified	genomic	141	ttcttaggtgtgNttttttttttt
142	IGR1070a_2	t/c		Verified	genomic	614	ttccatgttttcaNttggaatttatattttaatgt
143	IGR1070a_2	t/c		Verified	genomic	614	ttccatgttttcaNttggaatttatattttaatgt

144	IGR1070a_3	t/g		Verified	genomic	308	tctaactgtNtcttaaacgtg
145	IGR1071b_1	t/c		Not yet verified	genomic	115	ttattccattgttttcaNttggaatttatatttta
146	IGR1072a_1	t/c		Verified	genomic	337	ctgacatatatttatttaNttattagtattttttga
147	IGR1092a_1	a/c		Verified	genomic	241	aagcagagaccaNacatacatcacc
148	IGR1095a_1	a/g		Verified	genomic	148	agaaagggactNtctggagccagg
149	IGR1095a_2	g/c		Verified	genomic	213	ttttctctgccaNcatagtccttaigca
150	IGR1098a_1	a/c		Verified	genomic	237	gcaagccagaNgacagggccacag
151	IGR1098a_2	g/c		Verified	genomic	294	octgtctttgaatNcaaacgtcgtgc
152	IGR1099a_1	other/w +	Poly t	Verified	genomic	216	atgcatggcatgttcNttt
153	IGR1099b_2	a/g		Not yet verified	genomic	406	tagagacNgagtttcacc
154	IGR1099b_3	a/g		Not yet verified	genomic	270	ctggagtNcaatggcacg
155	IGR1100a_1	ins/del	deletion of 1 g	Verified	genomic	602	atgaaaaacttaacggNtcttcagctctgttctta
156	IGR1100a_2	a/t	t on ref. sequence	Verified	genomic	103	tgattttagaattttattNaaaaaaaglcaa
157	IGR1102a_1	t/c		Verified	genomic	605	ttttcttatNgcattttggct
158	IGR1102a_2	t/c		Verified	genomic	400	aattagccaggNgtgggagcgcgca
159	IGR1102a_4	a/g		Not yet verified	genomic	119	ctgacattaccagNggaaaaacaatggctg
160	IGR1102a_6	other/w +	Poly a	Verified	genomic	549	cgagactccatctggNaaa
161	IGR1103a_1	other/w +	Poly a	Verified	genomic	78	aaaNgagtttctctg
162	IGR1104a_1	g/c	g on ref. sequence	Verified	genomic	526	cagctcttatgttgNttttattctcag
163	IGR1105a_1	a/g	g in ref. sequence	Verified	genomic	383	ttaggttctttggaagcNggtttatgaactaat
164	IGR1107a_1	a/c	a in ref. sequence	Verified	genomic	402	aagattcaatgNaatcagtgacttgt
165	IGR1109a_1	a/g	a in ref. sequence	Verified	genomic	415	ggtagalgtgNtattacaagatg
166	IGR1110a_2	ins/del		Verified	genomic	195	aaaaaaNttattaccgg

any data upon which the data is based, and the data is not to be used for any other purpose.

167	IGR1111a_1	other/w +	Poly a	Verified	genomic	481		gagctagactctgtctcNaaa
168	IGR1111a_2	a/g	g in ref. sequence	Verified	genomic	318		tctactaaaNatacaaaaa
169	IGR1111a_3	a/g	g in ref. sequence	Verified	genomic	325		atacaaNaattagcc
170	IGR1112a_1	t/c	c on ref. sequence	Verified	genomic	183		aaatacaaatagaNaacatacaaaa
171	IGR1113b_2	a/c		Not yet verified	genomic	293		tacctgaNgtgtgtctg
172	IGR1114a_1	t/c	c on ref. sequence	Verified	genomic	254		gtggctcacacNtgcattccagcac
173	IGR1114a_2	a/g	a in ref. sequence	Verified	genomic	312		cccaggaagtcNaggctgcagtg
174	IGR1115a_1	other/w +	Poly a	Verified	genomic	465		gagccagactctgtcttNaaaaa
175	IGR1115a_2	a/c		Verified	genomic	307		cctctctactaaaNatacaaaaaattag
176	IGR1115a_3	t/c		Verified	genomic	322		atacaaaaaattagcNgggtgtgtgtggg
177	IGR1115a_4	g/c		Not yet verified	genomic	438		gaatgaactccagcNtgggtgacagagcc
178	IGR1116a_1	t/c		Verified	genomic	625		gacttaaggtaggcNctgaataaagccct
179	IGR1118a_1	a/g		Verified	genomic	192		gtatattgattagtaNgggtaatacattccaaatg
180	IGR1118a_2	other/w +	Poly a	Verified	genomic	47		ggcaaaaagagcgaaaactgtctcaaaaaaN
181	IGR1118a_3	t/c		Verified	genomic	619		agcctggctttgttctctaaNaagcctaaattgctag
182	IGR1119a_1	a/g		Verified	genomic	190		aa
183	IGR1120a_1	ins/del		Verified	genomic	258		ccaagctcctcatagNtctcattctgtctcag
184	IGR1126a_1	other/w +	Poly a	Verified	genomic	196		ttttctttttttNctgagacagttttttc
185	IGR1142a_1	ins/del	deletion of 2 bp	Verified	genomic	526		agagactcgtctcNaaaaa
186	IGR1142a_2	t/c		Verified	genomic	321		ttttctgcagtaatacNtattaaaaatttagattc
187	IGR1144a_1	t/c		Verified	genomic	435		cagaacctcattagcagNgaicacigataaag
188	IGR1144a_2	a/g		Verified	genomic	611		calcaacaaggtcttaNagaattcctaagg
189	IGR1145a_1	a/g		Verified	genomic	338		aaatgagaaaaatctaNaatgaatctctgt
				Verified	genomic			taicacttcttcagNataaagtctctaa

190	IGR1145a_2	g/c other/w		Verified	genomic	463	aacagggtatttaataatcttcacattNcagtaataaa gac
191	IGR1148a_1	poly T +		Verified	genomic	304	ttttagagNtttttt
192	IGR1157b_1	t/c		Not yet verified	genomic	301	aagtgcctggNataatacac
193	IGR1161a_1	t/c		Verified	genomic	221	cagtcctatatttcaaaNgagcaaacagaca
194	IGR1161a_2	t/c		Verified	genomic	662	aaactattttactaaaaNagaagtcctccatta
195	IGR1169a_1	other/w +	Poly a	Verified	genomic	384	aaactctatcttNaaaaaaaaaaaa
196	IGR1169a_2	a/c		Verified	genomic	454	tgtgtgcaNagtaagagaa
197	IGR1172a_1	t/c		Not yet verified	genomic	587	cctaacattaNttcaaaaataa
198	IGR1173a_1	a/t		Not yet verified	genomic	517	agtttttNaaattttt
199	IGR1185a_1	t/c		Verified	genomic	516	aaaaattaNaaaaatfagc
200	IGR1185a_2	t/c		Verified	genomic	576	aggctgaggNatgggaatc
201	IGR1186a_1	a/t		Verified	genomic	210	aacaagcttNcttttaaac
202	IGR1186a_2	ins/del		Verified	genomic	423	tttttttNagctctgattc
203	IGR1193a_1	a/g		Verified	genomic	343	atgcagcNatgtaaaaaa
204	IGR1196a_1	t/c		Not yet verified	genomic	109	aaaaaaacaNaaggcact
205	IGR1196a_2	a/g		Not yet verified	genomic	202	gaagggtcaNacaggaaag
206	IGR1196a_4	t/c		Verified	genomic	457	ggagcaaaaaNaaatgttta
207	IGR1199a_1	a/g		Verified	genomic	201	atatattccNagaaatgcat
208	IGR1199a_2	t/g		Verified	genomic	214	aaatgcatcaNlaggcaattt
209	IGR1200a_1	other/w +	Poly a	Verified	genomic	516	gacgacctttNaaaaaaaaaaa
210	IGR1218a_1	t/c		Verified	genomic	469	ttttaataacNtgataaatgcc
211	IGR1218a_2	a/g		Verified	genomic	590	gcctgctggNtagagagt
212	IGR1219a_1	t/c		Verified	genomic	129	gcittttaaaNttttct
213	IGR1219a_2	t/c		Verified	genomic	195	ctacaaagtNattttaaggg
214	IGR1219a_3	a/t		Not yet verified	genomic	251	ttttgctcaNagccttctt
215	IGR1258a_1	other/w +	gt repeat	Verified	genomic	177	taaaactatatataNgtgtgtgt

216	IGR1258a_2	t/c		Verified	genomic	436	ctcgggagtaNtggcacaca
217	IGR1279a_1	g/c		Verified	genomic	223	accagtaattattataaaatNaaagtaactaattgtt
218	IGR1279a_2	t/g		Verified	genomic	569	agccgggcggtgggcagNtgcctgtaatcccag
219	IGR1286a_1	g/c		Verified	genomic	365	ct
220	IGR1319a_1	a/c		Not yet			gtttgagaNagtctactct
221	IGR1350a_1	t/c		verified	genomic	200	taatttaaaggctctgNtccctgctcttttc
222	IGR1353a_1	g/c		Verified	genomic	125	acttcctcNtccccagg
223	IGR1353a_2	t/c		Verified	genomic	643	ctccaagggaNctcgtctcc
224	IGR1356a_1	ins/w+		Verified	genomic	438	tggatggaNggacgaac
225	IGR1362a_1	t/c		Verified	genomic	172	tagggaggNcattccag
			G in ref	Verified	genomic	434	caagggaagNgcatccag
226	IGR1363a_1	a/g	sequence	Verified	genomic	382	gcagtgggNcaagtggg
227	IGR1364a_1	del/w+		Verified	genomic	147	gttgttNgttttgag
228	IGR1365a_1	t/c		Verified	genomic	160	actgggatgNtcttaaacg
229	IGR1365a_2	ins/w+		Verified	genomic	211	gacttttNaatagagat
230	IGR1366a_1	a/g		Verified	genomic	371	caagacagtgNataaatagc
231	IGR1367a_1	a/g		Verified	genomic	73	aaagaaaaNtcagaattt
232	IGR1367a_2	del/w+		Not yet			ccctctccccNctctctc
233	IGR1369a_1	a/c		verified	genomic	425	tcaaaagagaNcaatgatga
234	IGR1369a_2	a/c		Verified	genomic	44	aaagtactaNtatgaaaat
235	IGR1370a_2	del/w+		Not yet			tatatataNacacacatac
236	IGR1370a_3	t/g		verified	genomic	350	gaagaaaNagtgcagtg
237	IGR1371a_1	t/c		Verified	genomic	241	aaaatagcNtcaggagtga
238	IGR1371a_2	a/g		Verified	genomic	72	aaaaaagNccaacagaaa
239	IGR1372a_1	other/w		Verified	genomic	231	tttttttNagggagagt
240	IGR1372a_2	+	poly t	Verified	genomic	298	ttctgtgctcNggctggagt
241	IGR1373a_1	t/c		Verified	genomic	323	aactagaaNtctccagg
242	IGR1375a_1	t/c		Verified	genomic	338	aggaattgaaNttaataga
243	IGR1376a_1	a/t	A in ref	Verified	genomic	96	cacttgNtgattaat
244	IGR1376a_2	del/w+	sequence	Verified	genomic	462	gcaagaagcNcaacaaacc
				Verified	genomic	79	

245	IGR1380a_1	other/w			Verified	genomic		573		agtcaccaacNttttt
246	IGR1380a_2	+			Verified	genomic		155		ttaatatgatNaatgtctcaa
247	IGR2001b_1	a/g			Verified	genomic		148		ccccacaaagNccgagaagcct
248	IGR2002a_1	a/c			Verified	genomic		357		aaaatcgagatgaaggNttgagcatttcagaga
249	IGR2003a_1	a/g			Verified	genomic		234		ttgcagtgagccNagatcacgtcact
250	IGR2004a_1	ins/del	bp	deletion of 14	Verified	genomic		576		tagagttgttcccNagagttgttccca
251	IGR2006a_1	t/c			Verified	genomic		122		ctttagtttcatcttNcctactgccca
252	IGR2006a_2	a/g			Verified	genomic		380		ctggctccNaattataaag
253	IGR2007a_1	other/w			Verified	genomic		459		taaagtaagaatcccctaaagttNaaaaa
254	IGR2008a_1	+		Poly a	Verified	genomic		646		aag
255	IGR2008a_2	t/c			Verified	genomic		596		ttactctgcaggagctNtagggagatgaaggaag
256	IGR2009a_1	g/c			Verified	genomic		270		aagcc
257	IGR2010a_2	ins/del		deletion of "c"	Verified	genomic		359		ccctggaggaggagcgtgNgggaaggaaatgac
258	IGR2010a_3	t/c			Verified	genomic		233		ac
259	IGR2010a_4	a/g			Verified	genomic		113		agagtaagtagggNccttaccacaggagcat
260	IGR2010a_6	a/g			Verified	genomic		329		agccttctgcttNcctcacttcccca
261	IGR2011a_2	a/g			Verified	genomic		43		ggtagggctactNttattttagtt
262	IGR2011a_3	a/g			Verified	genomic		153		ccgtgctacttNacccctgcaacggcg
263	IGR2011b_1	g/c			Verified	genomic		396		agcacacggggcaNggtaggcttctgcc
264	IGR2011b_2	t/c			Not yet	genomic		500		gggcgatcacctcNcctgcttctggg
265	IGR2013a_1	g/c			Verified	genomic		431		acagcctggggccNggggcgtctggc
266	IGR2015a_1	t/g			Verified	genomic		443		agacgtgcgccgagccccccgcaaNcgagggc
267	IGR2016a_1	a/t			Verified	genomic		366		caccggagccgtgccc
268	IGR2016a_2	a/g			Verified	genomic		120		CCACTCGGAGTCGCGCTNCGCGC
269	IGR2017a_1	t/c			Verified	genomic		412		GCCCTCACTGCAGCCCC
270	IGR2018a_1	t/c			Verified	genomic		245		aaaggattgaatttgagNgaaaagt
271	IGR2020a_1	a/c			Verified	genomic		568		ctcgagtagtctgtgggNtagatcttactaatg
					Verified	genomic		366		ggaagaagtcttacttccNgtgggtgctta
					Verified	genomic		120		acttcatttNtactgtgtccc
					Verified	genomic		412		ggtccctgagctcccNgagacaacatgcagaatt
					Verified	genomic		245		actg
					Verified	genomic		568		gtcagccaccattNagtaactgttctgtctg
					Verified	genomic		568		gagagagaaaaagatgNtcagaactccaccctggc
					Verified	genomic		568		ac

המחלקה המדעית של משרד הבריאות, תשפ"ב
 המעבדה לרפואה גנטית, תשפ"ב

272	IGR2020a_15	t/g		Verified	genomic	408	ttctcccgactngcacatccagt
273	IGR2020a_2	a/g		Verified	genomic	379	cccagcactgtcgccNigtgtgtcagcagcact ctccc
274	IGR2020a_3	t/c		Verified	genomic	362	accitggcttctgtNccccagcacgtcgcc
275	IGR2020a_4	a/g		Verified	genomic	301	gcagggtggtcggNggcgctgatgtcttgcac actaa
276	IGR2020a_5	a/g		Verified	genomic	210	caggctggcaggNgaccccacagggtcagtggg atgactc
277	IGR2020a_9	a/g		Verified	genomic	194	actccagggtgagctgNiccagggtcggc
278	IGR2021a_1	ins/del		Not yet verified	genomic	233	ggccagggtgcatttgNgggtgctgtctctcct c
279	IGR2021a_2	a/g		Verified	genomic	147	ccatagggggaggaagcgacNgggacacactag gaaggca
280	IGR2021a_3	t/g		Verified	genomic	197	ctgcagtacagtgggggctgNtgagagagggga aggg
281	IGR2021a_4	other/w +	gt repeat	Verified	genomic	394	gtgtgNcagagacagagagacagagagagaga g
282	IGR2021a_5	ins/del	deletion of 16 bp	Verified	genomic	277	gcccagcatctgagggNtaggggtgtaatacggc a
283	IGR2022a_1	t/c		Verified	genomic	612	aggtcaggagtNtagaccagcctgactaacatg gtgaaa
284	IGR2022a_2	t/c		Verified	genomic	439	aatcagccttaggatcNgtaatatgatggtcttt
285	IGR2022a_3	t/c		Verified	genomic	190	ctgtgtcacctggctgNtgcattgtccacaagtg c
286	IGR2022a_4	a/g		Verified	genomic	248	ggaaagccaccatNggaaggggaagccagg
287	IGR2024a_1	t/g		Verified	genomic	163	gccaaggggtgatactggctNagaggagctggc tca
288	IGR2024a_2	a/g		Verified	genomic	461	atggagaaagctggggggcaggNccaggggagc agg
289	IGR2024a_3	t/g		Verified	genomic	517	cacattggaattagctacNgctgccatgccttaag g
290	IGR2024a_7	a/g		Verified	genomic	468	gggcagggccaggNgcagggcggtaaa
291	IGR2025a_1	t/c		Verified	genomic	139	cctgaigccaccgtcccNtaccctcatacaac
292	IGR2025a_2	a/g		Verified	genomic	141	ctgatgccaccgtccctNccctcatacaaccttctt
293	IGR2025a_5	a/g		Verified	genomic	270	ttgccttcataccaNgccattccctgt

294	IGR2025a_6	a/g		Verified	genomic	377	aagctggactctgtNggccctcaac
295	IGR2026a_1	ins/del	deletion of "c"	Verified	genomic	244	cacaagaactaccccNtttcagctgagccc
296	IGR2026a_2	a/g		Verified	genomic	314	glgggtcctcggggcNattgtccctcagcctc
297	IGR2026a_3	ins/del	ins/del "a"	Verified	genomic	611	tcatgtgaaacacataNgacgtgtgtaaatatgta
298	IGR2027a_1	ins/del	ins/del "g"	Verified	genomic	166	aaagtaaatgtttataaNgggtgtggccttttagag
299	IGR2027a_2	a/g		Verified	genomic	291	gaacagggaatgcacatNttataaaatccttcg
300	IGR2027a_3	a/c		Verified	genomic	309	ttataaaatccttcggNcaggcgcggtggcgcaca
301	IGR2027a_4	t/c		Verified	genomic	386	ccfg
302	IGR2027a_5	other/w		Verified	genomic	562	tcaccgtgaggtcaggagttNgagaccagccttggtg
303	IGR2029a_1	a/g	Poly a	Verified	genomic	112	aaa
304	IGR2029a_2	t/c		Verified	genomic	166	actccagccgggaccNaaaaa
305	IGR2029a_3	other/w		Verified	genomic	180	tgaacccgggagatgNaggtgcagtgagct
306	IGR2030a_1	t/g	Poly a	Verified	genomic	539	tcacgcctgggtgacaagagNgagactttgtctca
307	IGR2031a_1	t/g		Verified	genomic	415	aa
308	IGR2031a_3	t/g		Verified	genomic	40	ttgtcaaaaaaaaaaaatcctttg
309	IGR2031a_4	a/g		Verified	genomic	227	gaaggtgtggatgtgcNtttctgtctcct
310	IGR2031a_5	t/g		Verified	genomic	232	gatgtgtgtgagtgaggcaggNggactcctgtctggg
311	IGR2032a_1	ins/del		Verified	genomic	126	ta
312	IGR2032a_2	a/g		Verified	genomic	356	tgtggatatgtgcNtttctgtctcct
313	IGR2032a_3	other/w		Verified	genomic	278	cicagtcaccagaaaccNtatgtactgtgac
314	IGR2033a_1	t/c	Poly a	Verified	genomic	587	cicagtcaccagaaaccatgtNacttgacccccgc
315	IGR2034a_1	t/g		Verified	genomic	441	tcact
316	IGR2036a_1	g/c		Verified	genomic	356	tcctactaaaaaNaactaaccaggcgtgtggg
317	IGR2036a_2	a/g		Verified	genomic	183	ggaacagaggNatagacagga
318	IGR2037a_1	ins/del	ct repeat	Verified	genomic	534	agactctgtctcNaaaaa
319	IGR2038a_1	ins/del	aaac repeat	Verified	genomic	532	atcattctaaggaNctgacagtgctcttg
320	IGR2039a_1	ins/del		Verified	genomic	394	gaagctaataNgcaaacatc
321	IGR2041a_1	a/g		Verified	genomic	331	acctcaaatgtggctggata
				Verified	genomic		gtaagacacaNgcctgcagag
				Verified	genomic		aagacaacctagtctNctgtctgtcttaaa
				Verified	genomic		tgaattctacagtggtNaaacaaaca
				Verified	genomic		tgttggctNgttggat
				Verified	genomic		cacgtattaaagccacacctacNatataccacc

322	IGR2042a_2	t/c		Verified	genomic	270		gagggccaaggcttgcctgccNctcctgccct
323	IGR2043a_1	a/g		Not yet verified	genomic	334		tcgatagtgccNggaacatcctgact
324	IGR2047a_1	other/w +	Poly t	Verified	genomic	225		tgtagggcttgcNtttt
325	IGR2049a_2	t/c	t on ref. sequence	Verified	genomic	332		gacccctgctfacatNgtacataacaatagctata
326	IGR2051a_1	t/c	t on ref. sequence	Verified	genomic	470		ggcagggNgtctggcaaggaccagtc
327	IGR2051a_2	a/g		Verified	genomic	605		acacitattNtaactgacccctgggccc
328	IGR2052a_1	t/c		Verified	genomic	290		gctatttctcNttgtattcgcagtgaccagg
329	IGR2052a_2	a/g		Verified	genomic	106		ttgacaaacactattNtaactgtcacc
330	IGR2053a_1	a/g		Verified	genomic	225		cattcactgtctgtcNgggctagagaaga
331	IGR2053a_2	a/c		Verified	genomic	369		cactgtctgtcgcagtgacNcctgtctccctaa
332	IGR2053a_3	t/c		Verified	genomic	544		gtgacccctattggaatctctcaNgccactgaggat
333	IGR2054a_1	t/c		Verified	genomic	196		at
334	IGR2054a_2	ins/del	ins/del 6 bp	Verified	genomic	591		caaggaggaatgagctttNgcagaggggctg
335	IGR2055a_1	t/g		Verified	genomic	609		cttctcttctctgtNcccttctgcctc
336	IGR2056a_1	a/g		Verified	genomic	153		gagtggtttgagaagaNctgaggagtgaggac
337	IGR2056a_2	a/c		Verified	genomic	364		tttttaagactagtcNctggcgcggt
338	IGR2056a_3	other/w +	Poly a	Verified	genomic	481		gagaatggcgtgaacccggaggNagagcttgc
339	IGR2056a_4	g/c		Verified	genomic	432		agt
340	IGR2057a_1	a/g		Verified	genomic	421		aagcgagactccatctcNaaaaaaacaaaa
341	IGR2060a_1	g/c		Verified	genomic	514		aaca
342	IGR2061a_3	t/c		Verified	genomic	236		gagctgcagtgagctgaNalcgcgcactgcact
343	IGR2062a_1	ins/del	caaa repeat	Verified	genomic	195		gaagtgaacacaaatNcaagggtacaga
344	IGR2063b_1	g/c	c on ref. sequence	Verified	genomic	218		ttgcaacccciNgcaaggtaa
345	IGR2063b_2	t/g	t on ref. sequence	Verified	genomic	369		catacacaagaaNgagtccattactg

346	IGR2064a_1	a/c		Verified	genomic	364	aactgtgatttNcagtttcaatt
347	IGR2064a_2	a/g		Verified	genomic	508	ccctcagagggcNgttactggact
348	IGR2066a_1	t/c		Verified	genomic	459	cttcattctccctgccaaNgaagctgggtggtgccc
349	IGR2067a_1	a/g		Verified	genomic	163	agccactacttgggcNgctcagctc
350	IGR2067a_2	a/g		Verified	genomic	243	cacacttctccacNagaataaagcaagca
351	IGR2067a_3	t/c		Verified	genomic	266	agcaagcagctgttNctctcttggccc
352	IGR2067a_4	a/g		Verified	genomic	485	agcctgagcctNgcgagcccagac
353	IGR2068a_1	other/w +	ca repeat	Verified	genomic	354	acacacacacaNtttttgagagagag
354	IGR2068a_2	g/c		Verified	genomic	70	atgtgtagtgtgagaaNgtgtgagaggtactcg
355	IGR2069a_1	a/g	g in ref. sequence	Verified	genomic	394	ttatgttcattgtacNttaccataattt
356	IGR2069a_2	t/c		Verified	genomic	425	atccactctcNtgtcatggacatcg
357	IGR2070a_1	t/c		Verified	genomic	551	tctaaagaaaaaagaaagcNgtgaattcttgac
358	IGR2071a_1	t/g	g on ref. sequence	Verified	genomic	165	gctctgtgccaggcaggggNctccgagggtgagtg
359	IGR2071a_2	a/t	a on ref. sequence	Verified	genomic	171	ccaggcagggggctccgNggtagtgtggcct
360	IGR2071a_3	a/g	a in ref. sequence	Verified	genomic	365	agagaaggggaactggcNtgtgtgcttggcgctgtg
361	IGR2072a_1	a/g	a in ref. sequence	Verified	genomic	312	gcaggctcagtgaaggagaggNgtctccttatg
362	IGR2072a_2	t/c	t on ref. sequence	Verified	genomic	408	atggggaactctctaNactgtggaggcggtg
363	IGR2073a_1	a/c	a in ref. sequence	Verified	genomic	94	agtcatggcactaNatggagcccaggg
364	IGR2073a_2	a/g	a in ref. sequence	Verified	genomic	313	caccaggaggttcagcNcccactgtgg
365	IGR2073a_3	t/c	c in ref. sequence	Verified	genomic	379	gcattcccagcgccNggccagtggtcc
366	IGR2074a_1	ins/del		Verified	genomic	239	gagtaaggggtcNaggaggggggggtggc
367	IGR2076a_1	t/c	t on ref. sequence	Verified	genomic	184	gaacatactcataNccatgctcccc
368	IGR2076a_2	other/w +	Poly t	Verified	genomic	647	tacacttatgtttgtgcNttttttt

369	IGR2077a_1	other/w +	Poly t	Verified	genomic	148	tatggttgTgcNtttttttt
370	IGR2078a_1	a/g	g in ref. sequence	Verified	genomic	197	gcagggtggggagaaNgccagacitcagggtg
371	IGR2078a_2	ins/del	ins/del "c"	Verified	genomic	67	ggcccagcccccccNggaagtgat
372	IGR2079a_1	ins/del	Poly a	Verified	genomic	345	gtaaaaaaaaNccctacaggtaaaag
373	IGR2079a_2	t/c	t on ref. sequence	Verified	genomic	582	cccccatgtccaNgicaccctccctgtc
374	IGR2081a_1	a/g	a in ref. sequence	Verified	genomic	140	cccagcaggaaacaNaitgcaca
375	IGR2081a_2	a/t	t in ref. sequence	Verified	genomic	315	gaaccagagagaccNgtaggagggg
376	IGR2081a_3	a/g	a in ref. sequence	Verified	genomic	622	gcccggcagagtcaccNgggctggcc
377	IGR2083a_1	t/c	sequence	Verified	genomic	372	aaatggggccaggNgcggtggtca
378	IGR2083a_2	ins/del	g in ref. sequence	Not yet verified	genomic	199	ccgtctataaaaaaaaNNNgtgggtgtgtg
379	IGR2083a_3	a/g	sequence	Verified	genomic	572	aatgtctgaacccNggaggcagaggtt
380	IGR2084a_2	ins/del	ccaa repeat	Verified	genomic	166	ccaaccaaccaNccaaatggtattaactctc
381	IGR2085a_1	t/c	c on ref. sequence	Verified	genomic	131	cacttacctgcccNgccccaccc
382	IGR2085a_2	a/g	a on ref. sequence	Verified	genomic	249	tcctcttgaacctNtgtgatttct
383	IGR2085a_3	a/g	a on ref. sequence	Verified	genomic	437	tgtcaacagtcaccaNctgagcccagcc
384	IGR2085a_4	a/g	sequence	Verified	genomic	368	cttgagggtgctcNtaagagggtccaatga
385	IGR2085a_5	t/c	sequence	Verified	genomic	538	ttattcagtcacctNgagtcattccagtc
386	IGR2087a_3	other	gaa repeat	Not yet verified	genomic	193	agggagaagaagaaNcaagaggaagagga
387	IGR2087a_4	other/w +	Poly a	Verified	genomic	504	gaaagccaaataaaaaaaaaNtcaacagaa
388	IGR2090a_1	a/c	a in ref. sequence	Verified	genomic	219	agtcaggctgtctcgccNgctaaaaagagcc
389	IGR2090a_2	t/c	sequence	Verified	genomic	360	tgcttggtggggctcNagcgttaaccg
390	IGR2090a_3	t/c	c on ref. sequence	Verified	genomic	444	ttcaccattgttctcNctattcccttt

המחלקה המדעית של משרד הבריאות
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391	IGR2090a_4	other/w +	Poly t	Verified	genomic	532		acttacctgctgaaatgcactgNttttttt
392	IGR2091a_1	t/g		Verified	genomic	581		taatgacattcccttgtaNgaatgtgccaatgtgga
393	IGR2091a_3	a/c	a in ref. sequence	Not yet verified	genomic	391		gatacattaNttgcctgagtt
394	IGR2091a_4	t/c		Not yet verified	genomic	404		ttgcctgagttcNcaagtgtgtaagaga
395	IGR2091a_5	ins/del		Not yet verified	genomic	547		tctcatcaataatattatNNNcttcatt
396	IGR2092a_2	ins/del	Poly a	Verified	genomic	435		aaaaaaaaaaaaNggcaggcgcg
397	IGR2093a_1	ins/del	Poly a	Verified	genomic	229		aaaaaaaaNgcctagaccctctg
398	IGR2093a_2	a/g	g in ref. sequence	Not yet verified	genomic	123		ttggaggcgtaggcNgaagaatcgct
399	IGR2093a_3	t/c		Verified	genomic	181		agattgtccactgNgctcagct
400	IGR2093a_4	a/g	g in ref. sequence	Verified	genomic	318		gggagaccggaggaggNtaggggaagtg
401	IGR2095a_1	t/c	c on ref. sequence	Verified	genomic	421		caacagcctggcagNgaggccctgtct
402	IGR2096a_1	a/c	c in ref. sequence	Verified	genomic	112		actagagggtttttaNagagaagtgcacatgat
403	IGR2096a_2	a/g		Verified	genomic	498		taaggaatacggtttgNacgtaagtgtgagatgcc
404	IGR2097a_1	a/c		Not yet verified	genomic	58		caggtggaanltgtgaatctctggggagag
405	IGR2097a_2	ins/del	Poly a	Verified	genomic	463		aagactctgtctcNaaaaa
406	IGR2101a_1	t/c		Not yet verified	genomic	283		cccagaatagagaccacNtccatctctccitt
407	IGR2102a_1	g/c	g on ref. sequence	Verified	genomic	166		gaacttagatttgcgNcccttagcattcaac
408	IGR2102a_2	t/g	g on ref. sequence	Verified	genomic	223		caatgcatgatctcNtctgagccctcagc
409	IGR2105a_1	a/t		Not yet verified	genomic	493		ttgatactcagtaNgtacagcttatt
410	IGR2106a_1	other/w +	ct repeat c on ref.	Verified	genomic	137		caggcaacaaaaNtctccctccct
411	IGR2107a_1	t/c	sequence	Verified	genomic	300		ccttgctcaaNtgctcagctctatc

Genomic DNA sequences for the 1000 Genomes Project, 2010. The sequences are from the human genome, and are used to identify genetic variation in the population.

412	IGR2107a_2	t/c	t on ref. sequence	Verified	genomic	564	ccaaaggctcNcaggctctggc
413	IGR2108a_1	ins/del		Verified	genomic	360	ccattccctgagcNcaggltgccttct
414	IGR2109a_1	a/g		Verified	genomic	400	ggccaggctggtctcNgtctagactcaagtg
415	IGR2110a_1	t/c		Not yet verified	genomic	286	tgtttgagacaggggtctgNtctgtctcaggatgg
416	IGR2110a_2	other/w +	Poly t	Verified	genomic	420	atgccagctaNttttt
417	IGR2111a_1	a/g		Verified	genomic	55	ccaccgcaccggccaNttttattgttttlaaa
418	IGR2111a_3	t/c	c on ref. sequence	Verified	genomic	516	ttgccaacatttggtatNatcagltctcaatttt
419	IGR2112a_1	other/w +	Poly t	Verified	genomic	285	ttttttttNctgagacagagtcgcgt
420	IGR2114a_1	other/w +	Poly a	Verified	genomic	3331	caattgacttccctNaaaaa
421	IGR2117a_1	a/g		Verified	genomic	355	aagggtgacctagNgcacacacitccctccc
422	IGR2121a_1	other/w +	Poly a	Verified	genomic	609	aataaagtgattactNaaaaaaaaaaaa
423	IGR2121a_2	a/t		Verified	genomic	117	gagggcctgacagNtgaagggttg
424	IGR2121a_3	t/c		Verified	genomic	815	ccctgggggtNtttccaaatca
425	IGR2123a_1	a/g	g in ref. sequence	Verified	genomic	230	ttgccagaacacNgggtcagagagcaagag
426	IGR2125a_1	other/w +	Poly a	Verified	genomic	546	agagtgagactctgtctcaaaaaaaaaaaaa
427	IGR2126a_1	a/g		Verified	genomic	364	cttcatactacttNgaaaaccatat
428	IGR2126a_2	other/w +	Poly a	Verified	genomic	47	gagactctgtctcNaaaaa
429	IGR2131a_1	other/w +	Poly a	Verified	genomic	249	aaaaaaaaaaaaNgaacctctgtcgtat
430	IGR2134a_1	a/g	a on ref. sequence	Verified	genomic	339	acttcagattaataNgtcttaaccat
431	IGR2136a_2	t/c		Verified	genomic	444	tgtctgtagctccatttgagNaggacctt
432	IGR2138a_1	a/g		Verified	genomic	375	atgatttgcNtcaaaagcag
433	IGR2144a_1	t/g		Not yet verified	genomic	384	tcagtagcacatctgtNtttccatgctctt
434	IGR2144a_2	other/w +	Poly a	Verified	genomic	463	acagaggtaaagtgttttgaaagcNaaaaa

435	IGR2144a_3	a/t		Verified	genomic	127	ctagcctaNggictaggccc
436	IGR2144a_4	t/c		Verified	genomic	137	ggctagggcNctctgcctg
437	IGR2144a_5	a/g		Verified	genomic	166	ggaatcattacNtatcaaatca
				Not yet verified	genomic	354	accatggatgcNtagctgagttcctg
438	IGR2147a_1	a/g		Verified	genomic	253	acagttgtccctNagcatcttcgagga
439	IGR2148a_1	t/c		Not yet verified	genomic	619	gagacttcattctNaaaaacaaaaacaaaaa
440	IGR2148a_2	other/w +	caaaaa repeat	verified	genomic	90	caaaaa
441	IGR2150a_1	g/c		Verified	genomic		aaactctaccacNactgaaatctgttta
				Not yet verified	genomic	336	ccctggggctctaNtatttggtgttac
442	IGR2150a_2	t/g		Verified	genomic	558	gaaagatataNaaattaaattaaa
443	IGR2150a_3	t/g		Verified	genomic		
		other/w +		Verified	genomic	202	aaaaaNtataccaattagttctcacttaa
444	IGR2151a_1	a/g	Poly a	Verified	genomic	566	catcttgcaNccccagcttc
445	IGR2151a_2	a/g		Verified	genomic	423	cagaacaaattagagaaaaactccNgtcaggctc
446	IGR2153a_1	a/g	a on ref. sequence	Verified	genomic		tccac
447	IGR2154a_1	a/g		Not yet verified	genomic	389	acaacaacgggtaNatatttttaggtctc
448	IGR2155a_1	a/c		Not yet verified	genomic	398	attatttagtcNaataatcacc
449	IGR2155a_2	a/g		Not yet verified	genomic	619	aaggcggggtNcagtggtcac
450	IGR2156a_1	a/c		Not yet verified	genomic	176	ctgaggcaggiggatcatNtgaggtcagg
451	IGR2157a_1	a/c		Verified	genomic	254	tggaagagacatgcatNcaaaccataic
		other/w +		Verified	genomic	411	tttttttttNccgtgaacag
452	IGR2159a_1	other/w +	Poly t	Verified	genomic	601	acaggcgcgcnacacacacacacaca
453	IGR2160a_1	other/w +	ca repeat	Verified	genomic	213	taaaaattattcgNgagaatttttagaa
454	IGR2160a_2	a/g		Not yet verified	genomic		
455	IGR2160a_3	a/g		Not yet verified	genomic	287	ccaagttacctggNctgtactgagagatga
456	IGR2162a_1	a/c		Not yet verified	genomic	350	acaaacaaaaaNaacacaccttatt

457	IGR2162a_3	t/c		Not yet verified	genomic	450		aaatatagNcaaaatact
458	IGR2164a_1	a/t		Not yet verified	genomic	557		tcctggccaacNtggtaaacccc
459	IGR2165a_1	ins/del	Poly a	Verified	genomic	473		ggaaaaaaaNcacacatgat
460	IGR2165a_2	ins/del		Not yet verified	genomic	271		ataaaaaaaaNgatttattgt
461	IGR2166a_2	a/c		Not yet verified	genomic	323		agtttcNgtttagaaaag
462	IGR2167a_1	t/c	c on ref. sequence	Verified	genomic	324		acttaagagaNcaaaataat
463	IGR2167a_2	a/t		Not yet verified	genomic	207		ttttaaaactNtaaaggaat
464	IGR2168a_1	ins/del		Not yet verified	genomic	341		tgttctttttcttcttNtttttagacggag
465	IGR2175a_1	a/g	g in ref. sequence	Verified	genomic	310		tggggccaaaaatctcNctgacttcagtg
466	IGR2175a_2	a/g	g in ref. sequence	Verified	genomic	526		tcccaaggtcacatNgttactatgtatgt
467	IGR2176a_1	a/g	g in ref. sequence	Verified	genomic	119		gaagcaagactgtcNggaacacTggactc
468	IGR2176a_2	a/g		Not yet verified	genomic	399		aaccatctgttgTgtcNtgaggctctctgtat
469	IGR2177a_1	a/c	c in ref. sequence	Verified	genomic	325		tgatgatcacgcaacNcagctgaagaatgat
470	IGR2178a_1	a/g		Verified	genomic	138		ccatcctaataatacacaagatgcNtttgacgctata
471	IGR2179a_1	a/g		Verified	genomic	284		aga
472	IGR2179a_2	other/w +	Poly t	Verified	genomic	371		aaagTcaaaaaatcNaaaggagatgagca
473	IGR2179a_3	ins/del		Not yet verified	genomic	470		ttctgggaaaaaggaaagtcNttttttttt
474	IGR2180a_1	a/g		Not yet verified	genomic	65		taatctctgcctccaggNtcaagtgatcttct
475	IGR2180a_2	g/c		Verified	genomic	383		gtatttttagtagagacNgggttctctatgtt
476	IGR2181a_1	other/w +	Poly t	Verified	genomic	260		tcaccagcaacctgttNtgagTgaatcatc
								aaaaagttttttttttNctaccaaaatgtacag

477	IGR2181a_2	t/c		Verified	genomic	416	attacattataattacaNgcatgatctaat
478	IGR2181a_3	a/g		Verified	genomic	614	ccaagaaagaggNtgtcatggggttaa
479	IGR2181a_4	a/c		Verified	genomic	83	gtggaggcctgaNagtaggcgagttt
480	IGR2182a_1	a/g		Verified	genomic	115	tgccctcaagaaaaggNtgtcatggggttaaacc
481	IGR2184a_1	other/w +	Poly t	Verified	genomic	58	tcccttcatcttagccigaaagactccccttagcaNtttt
482	IGR2184a_4	a/t		Not yet verified	genomic	448	tgccatgttgtNtgtcgcaccc
483	IGR2184a_5	ins/del	ins/del t	Verified	genomic	380	tattttttttttaagtaacNttaagttctagggt
484	IGR2185a_2	t/c		Not yet verified	genomic	420	gtctagatccNtgaggaaac
485	IGR2185a_3	t/g		Not yet verified	genomic	453	ttccacaatggtNgaactagttt
486	IGR2186a_1	a/t		Not yet verified	genomic	184	gtctatatacttNtccccgtgtt
487	IGR2188a_1	t/c		Not yet verified	genomic	549	tttgtgaagttgNttatcaacttaa
488	IGR2189a_1	a/g		Verified	genomic	475	ataigatgcattacNttatcgatttg
489	IGR2189a_2	t/c		Verified	genomic	252	cctgtctgtgctcNgggtttcaa
490	IGR2190a_2	t/c		Not yet verified	genomic	343	ttattgccNcaattc
491	IGR2190a_4	a/g		Not yet verified	genomic	326	ttggttgataNgctattaatta
492	IGR2191a_1	a/g		Not yet verified	genomic	286	tgttgattttNgatgtttcc
493	IGR2191a_2	t/c		Not yet verified	genomic	353	actgctttgaatgNgctccagattc
494	IGR2191a_3	a/g		Not yet verified	genomic	390	ttgtgtcttgtctctNttggtttcaaa
495	IGR2191a_4	a/t		Not yet verified	genomic	498	gcggttttgaNtgagtttctt
496	IGR2192a_1	t/c		Not yet verified	genomic	515	tttttttgNtttccatttgc
497	IGR2192a_2	t/c		Verified	genomic	506	ccccgcNttttttg
498	IGR2192a_3	t/g		Verified	genomic	359	tttatgaatcgggNgctcctglatt
499	IGR2193a_1	t/g		Verified	genomic	361	ttcaggagctcttNtaaggcagg

499b ccttg ccttg ccttg ccttg ccttg ccttg ccttg ccttg ccttg ccttg
 tttttt tttttt tttttt tttttt tttttt tttttt tttttt tttttt tttttt tttttt

500	IGR2193a_2	t/g		Verified	genomic	376	ggcctggNggtgacaaa
501	IGR2193a_3	t/c		Verified	genomic	423	atattattcNccttcacttat
502	IGR2194a_1	a/g		Verified	genomic	57	cagagagatccNctgttagtctga
503	IGR2194a_2	a/g		Verified	genomic	196	agagtatctttNtggtgtctctg
504	IGR2194a_3	t/c		Verified	genomic	220	attctcgaanltgaatgttgcc
505	IGR2197a_1	other/w		Not yet			
506	IGR2198a_1	+		verified	genomic	498	gtctaactagtcccaNcgagatgagccgggt
		g/c		Verified	genomic	233	cagtagacgaacNatgcaaaatacca
507	IGR2198a_3	a/t		Not yet			
508	IGR2199a_1	t/c		verified	genomic	98	tctggggctttNacgttttttagtg
509	IGR2200a_1	a/c		Verified	genomic	357	cagagataagaaNtagtttccaagaa
510	IGR2202a_1	t/c		Verified	genomic	176	acaggcttNgacagaggacttga
				Verified	genomic	308	tcaciaaatctagaaaNaaagattctaggcagt
511	IGR2202a_2	a/t		Not yet			
512	IGR2202a_3	a/g		verified	genomic	330	taggcagtgctgNtatttaaaaaaatcat
				Verified	genomic	528	caggactaaagtgaNctactctgaaaga
513	IGR2202a_4	ins/del	12 bp deletion	Not yet			
514	IGR2203a_1	a/g		verified	genomic	622	tttttgacacacacaatgacactNcacttagagaa
		other/w		Verified	genomic	329	gtgc
515	IGR2203a_2	+	Poly a	Verified	genomic	216	acaaacaataaacaNtaaaaaaaccacaca
516	IGR2204a_1	ins/del		Not yet			
				verified	genomic	584	cagagtattctgtgttNaaaaaaaaa
517	IGR2206b_1	t/g		Not yet			
518	IGR2207a_1	a/c		verified	genomic	520	acagcaaggccttNactgaaggactc
519	IGR2209a_1	t/g		Verified	genomic	428	agggcggtgtcagNagaagagctgggcc
520	IGR2209a_2	g/c		Verified	genomic	153	ggttataataatttNcgttcatcagacctc
521	IGR2209a_3	a/g		Verified	genomic	234	tgtaggggaaggNctatagccaagat
522	IGR2210a_1	g/c		Verified	genomic	462	gcacttctcaaNcttgagagaccaccag
				Verified	genomic	297	ggccatcagaatctcNagttgatctctaa
				Verified	genomic		tctgctaaggNtctgtgaggccc
523	IGR2210a_2	t/c	c on ref.	Verified	genomic	610	catctagggtgtaNgttccatgaggg
524	IGR2213a_1	g/c	sequence	Verified	genomic	314	cggtaactgtggagcaNagaggtggctccaa
525	IGR2214a_1	a/t	a on ref.	Verified	genomic	318	taaccaccagggtccagaNgtcgcctagaatcc
526	IGR2215a_1	a/g	sequence	Verified	genomic	198	cag
				Verified	genomic		agatctggagagattccccacNagagtcatatttc
							cc

527	IGR2221a_1	other/w		Not yet	genomic	214	cagagactttgtctgagNaaaaaaaagaaaaa
528	IGR2221a_2	a/t		Verified	genomic	261	gaaaaaaaggaaaaaattagcatgttta
529	IGR2221a_3	t/g		Verified	genomic	289	gctatcaatatcaaggcactgtgagNgctctatggat
530	IGR2221a_4	ins/del		Not yet	genomic	231	aaaaagaaaaaNaagaaaa
531	IGR2221a_5	t/c		Not yet	genomic	79	aaaaattagccaagtgNggtggcaggcac
532	IGR2222a_1	a/g	g in ref. sequence	Verified	genomic	446	gcacatgggggcacaNggicacactcacca
533	IGR2222a_2	t/c	c on ref. sequence	Verified	genomic	476	cagagtgccacgcaNagcaccgcccgcat
534	IGR2223a_1	ins/del		Not yet	genomic	194	tttttggttcctcctatttaaNatggtatctttgtga
535	IGR2223a_2	other/w		Not yet	genomic	485	gccicaaggNaagaatatt
536	IGR2224a_1	a/g	at repeat	Verified	genomic	300	ctccaaccatgccNccctttcttggggc
537	IGR2224a_2	t/c		Verified	genomic	387	gagtcctagtaattgacNaccaagtactaagac
538	IGR2224a_3	t/c		Verified	genomic	389	cctagtaattgactaNaagtactaagaccacaa
539	IGR2224a_4	t/c		Verified	genomic	582	tgaggacatcacagNtgtctccagaaaggta
540	IGR2225a_1	a/c		Verified	genomic	464	agtcgggtctcaNagtgtccatgtatt
541	IGR2226a_1	a/g	g in ref. sequence	Verified	genomic	204	taaagagaaagaaNcattgtctctgatt
542	IGR2226a_2	t/g		Verified	genomic	426	catgcttctatgtgtctNgccaaaaggactgaa
543	IGR2226a_3	t/c	t on ref. sequence	Verified	genomic	524	ggaatgtgtgaaNtgcatcatcagtgt
544	IGR2226a_4	t/c		Verified	genomic	272	taagaggtagtatcaNgtacaaaaagtattct
545	IGR2228a_1	g/c	g on ref. sequence	Verified	genomic	450	gatattcacagtatagtgNggaagaccaacatta
546	IGR2229a_1	t/g	t on ref. sequence	Verified	genomic	298	ttttctgtgtgttNttttttccatcac
547	IGR2230a_1	t/c		Verified	genomic	608	catacttttagccaNttagggtgtatt
548	IGR2233a_1	g/c	g on ref. sequence	Verified	genomic	597	tgtgaacctgtgggNaagtatttaa
549	IGR2234a_1	a/g		Verified	genomic	362	taatccagcaactcNggaggctgagaca

550	IGR2234a_2	g/c	g on ref. sequence	Verified	genomic	395	gaatcttgaacctgNgaggcagaggtgca
551	IGR2235a_1	t/c		Verified	genomic	153	gtgttcacatgtgNcatgtggcaagga
552	IGR2235a_2	t/g		Verified	genomic	386	agttaaagctttaNaattatacaat
553	IGR2236a_1	a/g		Verified	genomic	256	ttacctagtaaacccgNtcaagatacatca
554	IGR2236a_2	ins/del		Not yet			
555	IGR2236a_3	t/c		verified	genomic	321	attgaattacggagtcagatNttggctcttact
556	IGR2237a_1	a/g		Verified	genomic	441	gaagggcaggcacaNgtctctcctcagtc
557	IGR2237a_3	a/g		Verified	genomic	395	agcaaggcctctaacNctgtctcctaaatc
558	IGR2238a_1	a/g		Verified	genomic	619	tggccaatgacccccNggctcttttggac
559	IGR2238a_2	a/c		Verified	genomic	92	ccgtctctgctcNggttccaccctg
				Verified	genomic	115	accctggccaatgaNccccgggtcctttt
560	IGR2238a_3	ins/del		Not yet			
				verified	genomic	247	gctccacctctactattNactcttccaacct
561	IGR2238a_4	a/g		Not yet			
				verified	genomic	442	tggatctggctNcgccctgcctaaaca
562	IGR2239a_1	a/c		Not yet			
				verified	genomic	256	ctgtctccgcactgNtggcagtggtgg
563	IGR2240a_1	t/c		Verified	genomic	545	agtgtcatatttgagaNagggcccagagcat
564	IGR2242a_1	t/g		Not yet			
				verified	genomic	119	gtgggttaagatNgggtcacgagtcta
565	IGR2243a_1	a/c	c in ref. sequence	Verified	genomic	256	tgccccctgtatNgaagagagggc
566	IGR2244a_1	other/w +	Poly t	Verified	genomic	220	tttttttttNggctccctgaccc
567	IGR2244a_2	g/c	c on ref. sequence	Not yet			
			t on ref. sequence	verified	genomic	73	ccaccagcctggNraattttgt
568	IGR2244a_3	t/c		Verified	genomic	469	gaggtcaagNtccaggctctct
569	IGR2244a_4	t/c		Verified	genomic	576	tgagggtctctNcatctcttaaga
570	IGR2245a_2	a/g		Verified	genomic	145	aggacaatgggNagggagtggag
571	IGR2245a_3	a/g	g in ref. sequence	Verified	genomic	397	attacaggcccccNccaccacgcaggg
572	IGR2245a_4	t/g		Verified	genomic	434	atttttagcggaNacgaggtttcacca
573	IGR2245a_5	t/c		Verified	genomic	574	tgtctgtccaNaggtctggacag
574	IGR2245a_6	ins/del	Poly t	Verified	genomic	261	tttttttttNgagacggag
575	IGR2246a_1	ins/del		Verified	genomic	629	ccaccacgcccctgccaNtatttatta

576	IGR2248a_1	t/g	t on ref. sequence	Verified	genomic	145	ctagatgcagtgNtcagcaggccag
577	IGR2249a_1	a/g	a in ref. sequence	Verified	genomic	289	aactgaaNgttcaattcct
578	IGR2250a_1	t/c		Verified	genomic	145	ggctcagcaccacaNccagcaggcctt
579	IGR2250a_2	t/c	t on ref. sequence	Verified	genomic	253	ttctgtctgcgaNtggggccttca
580	IGR2250a_3	t/g	t on ref. sequence	Verified	genomic	302	acaccctaggctcacNgagaggccctcc
581	IGR2250a_4	t/c	c on ref. sequence	Verified	genomic	389	taicaatgaggggctaNtcacigggctacttac
582	IGR2251a_1	g/c	c on ref. sequence	Verified	genomic	269	taatccagcttggNaggcagaagcagg
583	IGR2251a_2	a/t		Verified	genomic	360	aaacacaaaaatNgcitgggctgtgtgg
584	IGR2251a_3	a/g	g in ref. sequence	Verified	genomic	392	cagctactcggagNctgaggcaggag
585	IGR2251a_4	g/c		Verified	genomic	436	aggcgaagattgcaNtgagccaagaacg
586	IGR2251a_5	+	Poly a	Verified	genomic	526	tgacagaggagagactgtctctctNaaaaaa
587	IGR2252a_1	a/g		Verified	genomic	323	cccaactagagtaaNtcttgacacacag
588	IGR2252a_2	t/c		Verified	genomic	405	tggccatcaggaNgggaggccagactg
589	IGR2253a_1	a/g	g in ref. sequence	Verified	genomic	246	ccggctccagcccNagcgcgagaa
590	IGR2254a_1	t/g		Verified	genomic	68	agcgggctgggggtcNgggaacgcgg
591	IGR2255a_1	a/c		Not yet verified	genomic	477	ttctagtagccNtattaataaaatt
592	IGR2255a_2	a/g		Verified	genomic	217	gaggctgggagctNtgacttttcatt
593	IGR2255a_3	+	Poly a	Verified	genomic	387	tcagaagctaacctggNaaaaaaa
594	IGR2256a_1	t/c		Verified	genomic	510	atcatagtcaccgcagNcctgaactcctaagctt
595	IGR2256a_2	+	Poly a	Verified	genomic	344	ttctcaggattgNaaaaaa
596	IGR2256a_3	a/g		Verified	genomic	179	tgaataaactttaNtggtatatttaa
597	IGR2257a_1	a/g	g in ref. sequence	Verified	genomic	423	atataatgtgtgNgtaaagaatat
598	IGR2257a_2	t/c	t on ref. sequence	Verified	genomic	508	cagcagatttttaaNaaggaaatctaa

any gaps are indicated by dashes (-) in the sequence. The sequence is shown in the 5' to 3' direction.

599	IGR2257a_3	g/c other/w		Verified	genomic	621	ctattcttactctcNtgaagatggtgg
600	IGR2258a_1	+ other/w	Poly t	Verified	genomic	575	tgcaNttttttt
601	IGR2259a_1	+ other/w	Poly t	Verified	genomic	234	gctaNttttttg
602	IGR2260a_1	t/c		Not yet verified	genomic	582	tcaacaataNgttaaat
603	IGR2261a_1	t/c		Verified	genomic	608	ggctgaggaggNggtaccc
604	IGR2262a_1	ins/del	Poly a	Verified	genomic	332	aagactccgctctcNaaaaa
605	IGR2262a_3	a/g	a in ref. sequence	Verified	genomic	425	ttcagagcNictgtccag
606	IGR2263b_1	g/c	g on ref. sequence	Verified	genomic	411	ttcaagtattctNctgtcagcctcc
607	IGR2264a_1	other/w +		Verified	genomic	318	taatagctgttttttNtgcacaaatcactgt
608	IGR2265a_1	t/c	c on ref. sequence	Verified	genomic	249	ccccacaattNggcttcaa
609	IGR2265a_2	t/c	t on ref. sequence	Verified	genomic	340	gtatagaaaaNgtaaatt
610	IGR2269a_1	a/g		Not yet verified	genomic	270	tagtacaagtatctNttgagtactgtct
611	IGR2272a_1	a/t		Verified	genomic	540	ttttaaaaaaaNtttaaggcatagga
612	IGR2272a_2	t/c		Verified	genomic	163	ctcttggaaggctgNggcagggaagatgc
613	IGR2272a_3	a/g	g in ref. sequence	Verified	genomic	384	taccacaaatatacaaaaaatagccNggcgtgtg g
614	IGR2272a_4	t/c		Verified	genomic	395	ttagccggggtgtgtgNgggcacctgtagtaccc
615	IGR2272a_5	g/c		Not yet verified	genomic	462	ttgtgaaccccgaggaggcgggNgttgaatgagt gagatt
616	IGR2273a_1	other/w +	Poly t	Verified	genomic	388	cccttatccacagNttttttttt
617	IGR2274a_1	t/g		Verified	genomic	311	tctcatgtcacgcgaNtcacatttgtgtgtg
618	IGR2274a_2	g/c		Verified	genomic	381	tcattagcttggcttNcattctctctgaac
619	IGR2274a_3	t/c	c on ref. sequence	Verified	genomic	539	atatctatgtgNcctttgtcttccg
620	IGR2276a_1	t/c	c on ref. sequence	Verified	genomic	113	cactactatctctNtgagcacaaaag

621	IGR2276a_2	a/c	c in ref. sequence	Verified	genomic	359	aaatgagtagcctcNtttgagagacagag
622	IGR2277a_1	a/g	a in ref. sequence	Verified	genomic	143	gatcatcgaaggttcNcaaaatcaagct
623	IGR2277a_2	other/w +	Poly t	Verified	genomic	485	gatgcaagaaNtttttttttttt
624	IGR2279a_1	a/g	a in ref. sequence	Verified	genomic	165	acaggatcacaccaccNtgccttgtaattt
625	IGR2279a_2	t/c	c on ref. sequence	Verified	genomic	256	catgtatctgccNgccctcagccctcctcaaa
626	IGR2279a_3	other/w +	Poly t	Verified	genomic	310	ccaatgcgcctggccNttttt
627	IGR2279a_4	g/c		Verified	genomic	108	cctctgccctccaggttNaagcagttctctcg
628	IGR2279a_5	t/c		Verified	genomic	277	gcctcctcaagtcNaggattacaggt
629	IGR2281a_1	a/c		Verified	genomic	144	cattctgcatiaNataaagaaatac
630	IGR2281a_2	other/w +	Poly t	Verified	genomic	87	aaattaattttttctccNtttttt
631	IGR2281a_3	a/t		Not yet verified	genomic	72	taattttttaaatNaattttttcttc
632	IGR2283a_2	ins/del	ins/del 2bp t on ref. sequence	Verified	genomic	574	cctggctctcNttagtatt
633	IGR2284a_1	t/c		Verified	genomic	486	gccttcactttccaNataccatcagc
634	IGR2284a_2	t/c		Not yet verified	genomic	536	tgccaagtactattNtaactcttgagaatac
635	IGR2285a_1	a/c		Verified	genomic	171	gaaaaatgaagcNggagaaaaatgaa
636	IGR2286a_1	a/c		Not yet verified	genomic	261	tgtctacatgcNagacaatca
637	IGR2287a_1	t/c	t on ref. sequence	Verified	genomic	107	cttgggaggcNgaggcaggcaga
638	IGR2287a_2	other/w +	Poly a	Verified	genomic	188	gtgaaaccccgctctactactaaaaataacNaaaa aaaa
639	IGR2287a_3	other/w +	Poly a	Verified	genomic	351	acagagcgagacccgctcNaaaaaaaaa
640	IGR2287a_4	t/c		Verified	genomic	463	tgttaaggactgggNtttcaaaaaatcig
641	IGR2287a_7	t/c		Verified	genomic	463	tatagaccatgNaaggactggg
642	IGR2288a_1	t/c	t on ref. sequence	Verified	genomic	170	atggcaaaagaNtttattgaca

643	IGR2288a_2	a/g	a in ref. sequence	Verified	genomic	198	ggatgtggagtacNagaggaagacagcc
644	IGR2289a_1	a/g	g in ref. sequence	Verified	genomic	215	cccaagtagctgggacNcaggtgtgtgccacca
645	IGR2291a_1	g/c	c on ref. sequence	Verified	genomic	153	ctgtaatcctagctactNggaggctgaggcatga
646	IGR2291a_2	a/g		Not yet verified	genomic	548	tagcaagaagNggaggagggtt
647	IGR2292a_1	a/c		Verified	genomic	256	gtctcatgtNatccccacc
648	IGR2292a_2	t/c	c on ref. sequence	Verified	genomic	589	tctatttatcttNaatttcctatt
649	IGR2292a_3	a/t		Verified	genomic	282	atggaattgtatcNtccctctttacaga
650	IGR2293a_3	ins/del	gt repeat	Verified	genomic	437	tgtgtgtgtNgtgtgtgtgtgtg
651	IGR2294a_1	t/c	c on ref. sequence	Verified	genomic	390	cctggaaaaaNgggacactcc
652	IGR2294a_2	t/c		Verified	genomic	440	ttagcaaatggNacaccagga
653	IGR2294a_3	t/g		Verified	genomic	481	tgcacagatccNatgtccatgga
654	IGR2295a_1	ins/del		Not yet verified	genomic	438	atttgcgttcNgcaatatgtgt
655	IGR2295a_2	a/g		Verified	genomic	535	tgcagctgaggNccctactggtagaa
656	IGR2297a_1	g/c	g on ref. sequence	Verified	genomic	65	taactcaagaaNattagagaaa
657	IGR2297a_2	t/c	c on ref. sequence	Verified	genomic	198	aaaacactcNtcaggata
658	IGR2297a_3	t/g	g on ref. sequence	Verified	genomic	487	ttcttaagaaaaNaatttcaacca
659	IGR2297a_4	t/c	c on ref. sequence	Verified	genomic	588	gattttgcaccacNaggcctgccctaaaaaga
660	IGR2297a_5	a/c	c in ref. sequence	Verified	genomic	446	ccctacaagccNgaagagag
661	IGR2298a_1	a/g	g in ref. sequence	Not yet verified	genomic	293	tttaaatgtaaatggNctaaatgtctca
662	IGR2299a_1	a/g	g in ref. sequence	Not yet verified	genomic	592	caaagacacaacNtgcagaatct
663	IGR2300a_2	t/c		Verified	genomic	606	ccaataacaggNtctgaaattg
664	IGR2303a_1	t/c	c on ref. sequence	Verified	genomic	189	ttttgtatctacNggcaaaatata

665	IGR2303a_2	g/c	g on ref. sequence	Verified	genomic	495	aatatctcattagNataatgagccc
666	IGR2304a_1	t/c		Verified	genomic	483	ctggatgttNgaatggcat
667	IGR2304a_2	a/g		Verified	genomic	667	ggttgagtgacatNacagggtaaaaa
668	IGR2305a_1	a/t		Verified	genomic	253	tttctggataggaaINcIgcataataatcatttgg
669	IGR2308a_1	t/c	c on ref. sequence	Verified	genomic	339	ttgtatcctttgtaagaaacNgctagtgggcca
670	IGR2308a_2	a/g		Verified	genomic	561	taggtattgtcaaaatgNactgcattataggaca
671	IGR2309a_2	t/c		Verified	genomic	610	gatgtgttttttttNtgagacgg
672	IGR2310a_1	ins/del		Not yet verified	genomic	273	aattttgtattttNtagtagagatgggt
673	IGR2311a_1	a/g	g in ref. sequence	Verified	genomic	181	gccagtcctggagtcNgtggcatgatgtgg
674	IGR2311a_2	a/c	c in ref. sequence	Verified	genomic	207	ttggctcacctgcaaNctccaccctcccggg
675	IGR2311a_3	ins/del		Not yet verified	genomic	525	caacctctgcctcctgggtNgcagttcctcctgcct
676	IGR2313a_1	other/w +	poly A	Not yet verified	genomic	499	aaaaaaaNcaactaag
677	IGR2313a_2	a/g		Not yet verified	genomic	370	taaccaggNtgtttcagg
678	IGR2313a_3	a/g		Not yet verified	genomic	335	aaatgggggNtggggaggaca
679	IGR2313a_4	t/c		Not yet verified	genomic	531	cagattaaaNcagtaaat
680	IGR2313a_5	ins/w+	C insert	Not yet verified	genomic	391	agtttggcNatgatagg
681	IGR2314a_1	ins/w+	varying number of GT repeats	Verified	genomic	560	atgttticaNgtgtgtgt
682	IGR2315a_1	a/g		Not yet verified	genomic	369	cttccattgcNaagagtttgc
683	IGR2315a_2	t/c		Not yet verified	genomic	533	taatttctaNgccctgtctt
684	IGR2315a_3	a/g	G in ref	Not yet verified	genomic	211	aacatgccNctgaaca

685	IGR2316a_1	a/g	G in ref	Not yet verified	genomic	499	cccaggcttNtaggatga
686	IGR2316a_2	t/c	G in ref	Not yet verified	genomic	565	aaaccctgNtctgataa
687	IGR2316a_3	a/g		Not yet verified	genomic	469	tgaataaNccccagtc
688	IGR2321a_1	t/c		Not yet verified	genomic		tttgaaaaNgtcaaatag
689	IGR3000a_1	a/g	a in ref. sequence	Verified	genomic	224	tttagaaNtgatacttt
690	IGR3000a_2	a/g		Verified	genomic	558	ttaagaaatatgNttctattactatc
691	IGR3002a_1	g/c	g on ref. sequence	Verified	genomic	146	ctgggcagNgttcgcaa
692	IGR3002a_2	a/g		Verified	genomic	511	atattgaacNacatagat
693	IGR3003a_1	a/g		Verified	genomic	494	tgaacccccNtcttactt
694	IGR3004a_2	t/c	c on ref. sequence	Verified	genomic	430	gagtgaaactctcacNgcccagatttcctc
695	IGR3004a_3	ins/del		Verified	genomic	285	attttctctcttNttttcttctct
696	IGR3005a_1	t/c	t on ref. sequence	Verified	genomic	494	aggagtagNtagatagaa
697	IGR3005a_2	g/c	c on ref. sequence	Verified	genomic	538	agtagcacNactaccca
698	IGR3005a_3	a/c	c in ref. sequence	Verified	genomic	34	cccatgaaggcaccacaaNtcaactgcccagt
699	IGR3006a_1	other	gt repeat	Verified	genomic	234	ccagttctgacgatactcNtgtgtgtgtg
700	IGR3006a_2	t/g		Verified	genomic	227	cagttctgacNatactcgt
701	IGR3007a_1	t/c		Verified	genomic	458	cgtagaccaNtgcgcca
702	IGR3007a_2	other/w +	Poly t	Verified	genomic	176	aaatactgtaccctgtgacNttttt
703	IGR3008a_1	t/c		Verified	genomic	147	cacttattaNttaccata
704	IGR3008a_2	a/c		Verified	genomic	339	tgcatagcaaNtctcactt
705	IGR3008a_3	t/c	C in ref sequence	Verified	genomic	342	atgcaacitcNcaacttcacc
706	IGR3013a_1	other	gt repeat	Verified	genomic	637	cacatttatatgcNtgtgtgtg
707	IGR3016a_1	a/g	a in ref. sequence	Verified	genomic	636	cigctggtacagctNgtgttcattttgc

Genomic coordinates are given in the format: chr:pos:ref:alt

708	IGR3018a_1	a/g	g in ref. sequence	Verified	genomic	238	gggcactgacacccNcctgtgtggggccc
709	IGR3018a_2	t/g		Verified	genomic	191	gggcacctgtgtcNtgatcgtttccttta
710	IGR3019a_1	a/g		Verified	genomic	205	ttgtgtagaaaaattttgccNattgtaggctaata
711	IGR3019a_2	a/g		Verified	genomic	388	cagctttattgaagaNgcaatgttacag
712	IGR3020a_1	g/c	g on ref. sequence	Verified	genomic	172	gtctctgcctcctggctNgttttttagctgtoc
713	IGR3020a_2	a/c	c in ref. sequence	Verified	genomic	349	cttacttagcctagaNaacaaattataag
714	IGR3020a_3	a/g	a in ref. sequence	Verified	genomic	542	tataggaaactacNataatgttagtca
715	IGR3022a_1	a/t	t on ref. sequence	Verified	genomic	267	gctggagagcttgNctcatctagcag
716	IGR3023a_1	g/c	c on ref. sequence	Verified	genomic	79	tcctcttagggcaNagtgcaggctccc
717	IGR3023a_2	ins/del	ct repeat	Verified	genomic	264	attctctctctNtctctctgtag
718	IGR3023a_3	t/g	g on ref. sequence	Verified	genomic	368	ggcatgacatatagcNcactgtaacttg
719	IGR3023a_4	t/c	t on ref. sequence	Verified	genomic	580	gggattacagggtgaaNcaccatacctggctaa
720	IGR3029a_1	a/g	A in ref. sequence	Verified	genomic	201	ctggagggtNcacagacagg
721	IGR3029a_2	a/g	A in ref. sequence	Verified	genomic	498	agtccaagNacaaagct
722	IGR3030a_1	t/c	T in ref. sequence	Verified	genomic	181	attcatgcNtgcctttt
723	IGR3032a_1	a/g	A in ref. sequence	Verified	genomic	158	actagggaNgccaaggc
724	IGR3032a_2	g/c	C in ref. sequence	Verified	genomic	281	gtaatccaNctattcggg
725	IGR3035a_2	a/g	G in ref. sequence	Verified	genomic	223	gtcaggggaNtgatggaaa
726	IGR3036a_1	a/g		Verified	genomic	187	aaatacaNtaaaataa
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			T in ref sequence	Verified	genomic		331	tcgtcacNgaagat
732	IGR3041a_1	t/c		Verified	genomic		435	caccctagaNatgatgggaa
733	IGR3042a_1	a/g		Verified	genomic		278	atagggccagtgatggNggctggcactgaact
734	IGR3043a_1	t/c		Verified	genomic		477	caggcatcaatgcagaNttagtgtttttcaggg
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736	IGR3044a_2	t/c		Verified	genomic		137	aagcatgggagcagtgtaaNcaaggacctgtgga aata
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738	IGR3046a_1	a/g		Verified	genomic			
739	IGR3047a_1	t/g		Verified	genomic		455	cagactctctccctNgccaggatattgcctttgt
740	IGR3047a_2	a/g		Verified	genomic		522	ttgactggcctgtgccNggactggggagagtaa
741	IGR3047a_3	t/c		Verified	genomic		609	gtgatgctctactcNgtcgcattacatagca
742	IGR3049a_1	t/c		Verified	genomic		437	ttatatacacctNattcgcagcacagaca
743	IGR3049a_2	t/c		Verified	genomic		611	gtccacgggcctgctgNttgccagacggggctcc a
744	IGR3050a_1	t/c		Verified	genomic		224	ttctgaatactgagatcNgaagaagtgtctcc
745	IGR3051a_1	a/t		Verified	genomic		667	tttagagatagaaggaaNggaaggctgttagat
746	IGR3053a_1	a/g		Verified	genomic		364	gggtcctttagaaaNggttttcttaggaa
747	IGR3053a_2	t/c		Verified	genomic		481	gttaacagtgcacatggNggggccagtgggagac a
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749	IGR3055a_1	t/c		Verified	genomic		375	ccctctctaccatNctccagcagaaggacag
		other/w +	Poly a	Verified	genomic		133	aaaaaaaaaaaaNttgcttaacatt
750	IGR3055a_2	a/g		Verified	genomic		328	ctcaaaaaagatgacaNtaatacctgtctctagg
751	IGR3056a_1	a/g		Verified	genomic		383	aaatacagtgaggcNctgcacacattacaggcc
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753	IGR3057a_1	t/g		Verified	genomic		94	tatatatatatatNtatttcacggtttgggtcta
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757	IGR3061a_1	t/c		Verified	genomic	362	tttcaattattgtataNtttactccagaagt
758	IGR3061a_2	t/c		Verified	genomic	592	caatatgtcatcaNactttaaagcatgacttc
759	IGR3062a_2	t/c		Verified	genomic	139	ttgaacatatataaNggtgccttatgccttaa
760	IGR3064a_1	t/c		Verified	genomic	616	cttgcaaggtatagtgacttcttgaataaa
761	IGR3065a_1	a/g		Verified	genomic	358	tttatccattttaatacaNggttctttttatgctgag
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764	IGR3072a_1	ins/del	caaa repeat	Verified	genomic	383	caacaaacaaacaaacaaNaactagccggg
765	IGR3072a_2	a/t	t on ref.	Verified	genomic	578	taaaataaaaaaNaacgaaaaataatt
766	IGR3078a_1	a/g	sequence	Verified	genomic	313	gggcaggagtgNaaagcactagag
767	IGR3079a_1	a/g		Not yet verified	genomic	120	cctccgaataaagtcNctctcagtatac
768	IGR3081a_1	t/g	t on ref.	Verified	genomic	317	gagtcctattcttctNggggtgcacaccg
769	IGR3081a_2	a/g	sequence	Verified	genomic	286	gaaacgacccagNaatgcgcctcg
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771	IGR3084a_1	t/c	t on ref.	Verified	genomic	504	cggcaggctgNcagagctt
772	IGR3086a_1	a/t	sequence	Verified	genomic	234	ttgagatggttNttggcgatgacc
773	IGR3087a_1	other/w	Poly t	Verified	genomic	325	ggaacaatctcNtttt
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776	IGR3088a_1	other/w	Poly t	Verified	genomic	108	tgataagctctcNtttttt
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778	IGR3089a_1	a/g	sequence	Verified	genomic	559	ctagaacaaaaaNgtaagaaaaa
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786	IGR3097a_2	a/c		Verified	genomic		373		acaacaacaaNaaaaagagctcaaatgg
787	IGR3098a_1	a/t		Verified	genomic		243		gtctttttaaaacNacaaatttatata
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824	IGR3152a_1	t/c		Verified	genomic	1223	gccgggcNgatagcct
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100% of the sequences were found to be identical to the reference sequence.

836	IGR3166a_2	other/w	poly t	Verified	genomic	651	ccatccttcNtttttt
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850	IGR3182a_2	a/t		Verified	genomic	620	aacacaaacNaaaaacaggccaa
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871	IGR3199a_1	other/w +	poly a	Verified	genomic	131	tgagctcNaaaaaaa
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873	IGR3201a_1	a/t	A in ref	Not yet verified	genomic	234	aggactNatctcta
874	IGR3203a_1	a/g		Verified	genomic	538	ctgctcNaggagcca
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GenBank accession numbers are shown in the left column. The accession numbers are shown in the right column. The accession numbers are shown in the right column.

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888	IGR3242a_1	a/g		Not yet verified	genomic	319	aacctaNggggaggg
889	IGR3244a_1	ins/w+		Not yet verified	genomic	91	tccgcNtgtgtct
890	IGR3248a_1	t/c		Not yet verified	genomic	395	actgtcNccaactt
891	IGR3252a_1	other/w +	poly T	Not yet verified	genomic	183	tctaccNtttttt
892	IGR3252a_2	t/g		Verified	genomic	136	g'gcgtNggactgaa
893	IGR3266a_1	a/g		Not yet verified	genomic	156	cagg'tggNatgtcttg
894	IGR3266a_2	a/g		Verified	genomic	185	ccac'tgggNccc'tggctt
895	IGR3268a_1	t/c		Not yet verified	genomic	367	tg'tt'gtaN'tctctcc
896	IGR3268a_2	t/c		Not yet verified	genomic	385	aggaactgNctcgacat
897	IGR3274a_1	a/g		Verified	genomic	126	ctctaggaNcatttcag
898	IGR3274a_2	a/g		Verified	genomic	284	tgcagaatNcag'tggagc
899	IGR3276a_1	other/w +	poly t	Verified	genomic	340	cttctctcNtttttttttt
900	IGR3276a_2	ins/w+	ins G	Verified	genomic	221	tttctgcgctNtgatttgg
901	IGR3278a_1	other/w +	poly t	Verified	genomic	69	cttcttctcNttttttttt
902	IGR3292a_1	other/w +	poly t	Verified	genomic	518	ttcatctcNtttttttttt
903	IGR3294a_1	t/c	T in ref	Verified	genomic	366	aatttatctcttcttcaagaaNttgaattttgaatct
904	IGR3298a_1	a/g		Not yet verified	genomic	76	gttccttcgNttttccac
905	IGR3300a_2	g/c		Verified	genomic	366	cctgagaggcatcaaaaNtcaaatatgatcaa
906	IGR3302a_1	a/g		Verified	genomic	218	catctatttgtatcNgtcacctgattggg

907	IGR3304a_1	ins/w+		Verified	genomic	319	tttggagggtgagggtgggNggatcaggaggtca ggag
908	IGR3310a_1	a/g		Not yet verified	genomic	361	ggaccaaNctgggggtg
909	IGR3310a_4	other/w +	poly a	Not yet verified	genomic	86	aaaaaaaaNgtttccc
910	IGR3312a_1	ins/w+		Verified	genomic	249	cagataagcatcagatttgNaaactacaatggga atg
911	IGR3324a_1	t/c		Not yet verified	genomic	388	tattgtattccaatNtggatglagccacca
912	IGR3326a_1	other/w +	tg repeat	Verified	genomic	261	tattcctagctgtggagaggNttttgtttgtttgtg
913	IGR3326a_3	t/g		Verified	genomic	295	ttgtttNtttagacagagtcica
914	IGR3328a_1	t/c		Verified	genomic	586	tatatatttagtttcatNtgaattcttctttgacc
915	IGR3330a_1	other/w +	poly t	Verified	genomic	200	tacctcNttttt
916	IGR3330a_2	other/w +	poly t	Verified	genomic	512	tttttttNaaccitaaa
917	IGR3332a_1	other/w +	Poly A	Verified	genomic	347	catctcNaaaaaa
918	IGR3336a_2	other/w +	poly a	Verified	genomic	467	aaaaaaaaNgagagag
919	IGR3340a_1	a/g		Not yet verified	genomic	524	agactaNcacagaaa
920	IGR3348a_1	t/c	T in reference	Verified	genomic	91	ccacatNctctcc
921	IGR3348a_2	a/g	A in reference	Verified	genomic	202	gatggtNagcatt
922	IGR3348a_3	a/g	A in reference	Verified	genomic	216	tttcatNtgtttt
923	IGR3348a_5	t/c		Verified	genomic	129	aatgatNgccatt
924	IGR3348a_6	a/g		Verified	genomic	264	gttcatNtcttg
925	IGR3348a_8	a/g	A in ref	Verified	genomic	618	gatttttNtataagg
926	IGR3348a_9	a/g		Not yet verified	genomic	584	tctaacNtttaag
927	IGR3350a_1	g/c	G in Reference	Verified	genomic	77	catgagNatggaa
928	IGR3350a_10	a/g		Not yet verified	genomic	451	cctgcctNattgccc
929	IGR3350a_11	t/c	C in reference	Verified	genomic	450	cctgccNaattgccc

genomic data from the reference genome (GRCh38) and the sample genome (HG001) for the region of interest (chr1:100,000,000-100,000,000). The data is presented in a table format with columns for the reference genome, the sample genome, and the variant call format (VCF) file.

930	IGR3350a_2	t/c	T in Reference	Verified	genomic	88	gaatgttNttccatt
931	IGR3350a_3	g/c	G in reference	Verified	genomic	236	gatttggNtctctg
932	IGR3350a_4	t/c	C in reference	Verified	genomic	247	tgtttgNctgttg
933	IGR3350a_7	t/c	C in reference	Verified	genomic	321	agttgcNtatcag
934	IGR3350a_8	g/c	C in reference	Verified	genomic	349	ggctgaNacaatg
935	IGR3352a_1	a/g	A in reference	Verified	genomic	282	gggacNgtgttg
936	IGR3352a_2	t/c	T in reference	Verified	genomic	314	ttattgNgtctat
937	IGR3352a_3	t/c	T in reference	Verified	genomic	330	attcttNtctctt
938	IGR3352a_4	a/g		Not yet verified	genomic	177	tgggagNgtgtat
939	IGR3352a_5	t/c	T on reference	Not yet verified	genomic	339	tcctttNttcttt
940	IGR3352a_6	a/g	G in ref	Verified	genomic	547	gtgtcaNttttgga
941	IGR3370a_1	+	poly t	Verified	genomic	354	ctttccNttttttt
942	IGR3370a_2	t/c		Verified	genomic	378	agacagNctgtctc
943	IGR3374a_1	a/t		Verified	genomic	193	ggctatNgaaaaa
944	IGR3378a_1	a/t		Verified	genomic	418	gcctgaNcataaag
945	IGR3378a_2	a/t		Verified	genomic	563	cttttNaaaaatagg
946	IGR3388a_1	a/t		Not yet verified	genomic	48	aatctttaNagtacatt
947	IGR3388a_2	other/w		Not yet verified	genomic	441	gttgaaatcNttttttttt
948	IGR3394a_1	t/c		Not yet verified	genomic	493	ccctacaNgtaaat
949	IGR3406a_1	t/c		Not yet verified	genomic	158	aaatataNacatttat
950	IGR3420a_1	a/g		Not yet verified	genomic	322	cgcctcNataaaa
951	IGR3428a_2	a/g	A in ref	Not yet verified	genomic	278	tataaggNtaagg
952	IGR3454a_1	t/c		Not yet verified	genomic	382	tccattNtgtaggtt
953	IGR3454a_2	t/c		Not yet verified	genomic	450	aattagaNcccattt

954	IGR3456a_1	a/g	G in Reference	Not yet verified	genomic	42	tcttcNttgtt
955	IGR3456a_2	a/t	T in Reference	Not yet verified	genomic	81	gtggttNgtagt
956	IGR3456a_3	t/c	T in reference	Not yet verified	genomic	108	ccttcaNgtcct
957	IGR3456a_4	a/g	G in Reference	Not yet verified	genomic	109	cttcatNtccct
958	IGR3456a_5	t/g	T in reference	Not yet verified	genomic	178	actcatNgttgg
959	IGR3456a_6	a/g	G in Reference	Not yet verified	genomic	179	ctcattNttggc
960	IGR3456a_7	other/w +	Poly T	Not yet verified	genomic	204	ctctctcNtttttt
961	IGR3456a_9	a/g		Not yet verified	genomic	398	catgtcNcctgcaaa
962	IGR3460a_1	g/c	C in Reference	Not yet verified	genomic	118	tttgNgcagag
963	IGR3462a_1	other/w +	poly t	Not yet verified	genomic	419	ttttttNgctcatca
964	IGR3466a_1	a/g		Not yet verified	genomic	185	gcctcatgNacccctacc
965	IGR3466a_2	g/c		Not yet verified	genomic	503	ctcacaaaNgctccagt
966	IGR3470a_1	a/t		Not yet verified	genomic	199	gctggaggNaggactag
967	IGR3470a_2	t/c		Not yet verified	genomic	438	gtcaaattNattcattt
968	IGR3470a_3	a/t		Not yet verified	genomic	178	tccagctgaNgatgcagg
969	IGR3470a_4	a/t		Not yet verified	genomic	214	agcccigaNtgggcacca
970	IGR3475a_1	a/c		Verified	genomic	483	cacccctgtNtatacact
971	IGR3475a_2	t/c		Verified	genomic	490	ctatacaNtggttggt
972	IGR3477a_1	t/g		Verified	genomic	468	ccaggtaagNtgcgtagtg
973	IGR3479a_1	a/g		Verified	genomic	178	tagtggNgagtcgggc

974	IGR3479a_2	a/t		Not yet verified	genomic	229	cgtacccaNtagtaaat
975	IGR3481a_1	a/t		Not yet verified	genomic	139	ctgggaggaNctggggact
976	IGR3483a_1	a/g		Verified	genomic	539	gtgatgggNtgccttaag
977	IGR3483a_2	t/g		Verified	genomic	495	atctggtaaNaggtgtgg
978	IGR3483a_3	a/c		Not yet verified	genomic	135	gaaacaggNgcgggtggca
979	IGR3485a_1	a/g		Verified	genomic	198	ctctgaaggNtcatcacag
980	IGR3487a_1	a/t		Not yet verified	genomic	184	ctctccaagcNcctgctagta
981	IGR3493a_1	a/c		Not yet verified	genomic	434	ctctttattaNtcccttccca
982	IGR3493a_2	t/c		Verified	genomic	517	gatgaaggaNtgggtcatgc
983	IGR3493a_3	a/g		Not yet verified	genomic	534	tgctaccaNgtgagcca
984	IGR3493a_4	g/c		Not yet verified	genomic	542	aggtaggccaNcaggatgag
985	IGR3495a_1	a/g		Not yet verified	genomic	195	tcacaacaNaagtcacag
986	IGR3499a_1	t/c		Verified	genomic	467	aggggtggactgtNattcttct
987	IGR3501a_1	other/w + poly T		Not yet verified	genomic	503	ttcatgaaagacNtttttttttttg
988	IGR3505a_1	t/c		Verified	genomic	213	tgcctctcNgggcttgggg
989	IGR3515a_1	a/g		Verified	genomic	604	agtggtgggatgNaacctccagc
990	IGR3515a_2	t/g		Not yet verified	genomic	440	ctccttcgNccaggtga
991	IGR3519a_1	t/c		Verified	genomic	230	tttctcctNccctgcctca
992	IGR3523a_1	t/c	T in ref	Verified	genomic	193	cacggccagNagcctcttg
993	IGR3525a_1	t/g		Verified	genomic	322	ttcagaggggtgNggctgggtcaagt
994	IGR3527a_1	t/c		Verified	genomic	87	cactgtggNctgagctcg
995	IGR3529a_1	a/g		Verified	genomic	251	catgtacagNgacagatctgg
996	IGR3529a_2	t/c		Verified	genomic	120	aagtgtctNtgaatgta
997	IGR3531a_1	t/c		Not yet verified	genomic	361	tcaacccctgNattctgtacaa
998	IGR3533a_1	a/g		Verified	genomic	137	cacagggagNgtttgaga

any other data may be used in the future for the purpose of this study.

999	IGR3535a_1				Not yet verified	genomic	462		ctgtcctNgtgggagga
###	IGR3535a_2				Not yet verified	genomic	363		tcgagcctgNctgatggcaaa
###	IGR3537a_1				Verified	genomic	426		ggagggttagNgcagaagtt
###	IGR3551a_1				Not yet verified	genomic	403		ggccatccaNcagaaac
###	IGR3553a_2				Verified	genomic	125		tcccccacNctgatcac
###	IGR3553a_3				Verified	genomic	426		gaattgcctaNggagtacgc
###	IGR3555a_1				Verified	genomic	188		actgcagccNgcactccca
###	IGR3563a_1				Verified	genomic	655		tccgggtcaNagtacct
###	IGRX100a_1				Not yet verified	genomic	142		accgtNataatc
###	IGRX320a_1				Not yet verified	genomic	383		tctaaacNgggggaaa
###	IGRX320a_2			poly t	Not yet verified	genomic	393		ggggaaacNttttt
###	IGRX460a_1			poly t	Not yet verified	genomic	292		tttttNgagatgga
###	IGRX610a_1				Not yet verified	genomic	684		attcctgNgtggcct
###	IGRX610a_2				Not yet verified	genomic	827		tttgctcNgctgcct
###	IGRX650a_1				Not yet verified	genomic	344		atcagggtNaigttta
###	IGRX660a_1				Not yet verified	genomic	203		tctagtgaNgacaccag
###	IGRX665a_1			poly A	Not yet verified	genomic	309		acagatcttNaaaaa
###	IL13_5240				Verified	gene	n/a	Interleukin 13	aaacttttcgcgaggacNgttcaacTgaacttc gaaagcatcat
###	IL13_5710				Verified	gene	n/a	Interleukin 13	ttggggaagacttggtgctNgcactTggagcca agggttcaga
###	IL13_5770				Verified	gene	n/a	Interleukin 13	agcactaaagcagTggaNcccaggagTccctggt aataagt
###	IL13_5940				Verified	gene	n/a	Interleukin 13	cgagtaattatgttttctNgtatttaaataataa tgtt

אנו מודים לך על שיתוף הפעולה שלך בנושא זה. אנחנו מקווים שתיהנה מההתנסות.

###	IL3_4400	c/t	Verified	gene	n/a	Interleukin 3	ccaagctccatgaccagacaacgNccttgaag acaagcigggttaactgctctaacaatga
###	IL4ex1_2495	c/t	Verified	gene	n/a	Interleukin 4	tcgttagcttctcgtataaactaatgNctcacattgt cactgcaaatgcacacct
###	IL4pro_1940	c/t	Verified	gene	n/a	Interleukin 4	acacclaaactgggagacaactgtNccccagtg tggggtaggaga
###	IL5pro3	c/t	Verified	gene	n/a	Interleukin 5	tgctcatgaacagataacataNagatccaggagt ctggacatcatc
###	IL9_4616	a/g	Verified	gene	n/a	Interleukin 9	tgtaaatggtgatgccaaacctgtttgaacNcaaa aggatgataaagtgtggaattggta
###	IL9_4616	a/g	Verified	gene	n/a	Interleukin 9	gtgaatgggtgatgccaaacctgtttgaacNcaaaa ggatgataaagtgtggaattgg
###	IL9_6085	c/t	Verified	gene	n/a	Interleukin 9	tctctgtaacagagccatgcaaccaaaccaNggca ggcaacgcgtgacat
###	IL9_6085	c/t	Verified	gene	n/a	Interleukin 9	cctgtgaacagagccatgcaaccaaaccaNggcag gcaacgcgtgacat
###	IRF1ex1_1	g/c	Verified	gene	n/a	Interferon regulatory factor 1	aagacgtgcgcgcagagccgcgcgaaNcgagg ccacccgagcgcgtgccagt
###	IRF1pro1_2	c/t	Verified	gene	n/a	Interferon regulatory factor 1	cacggggcagggtaggcttctgcttNcttcacttc ccaggggcaggtgagt
###	IRFex6_1	t/c	Verified	gene	n/a	Interferon regulatory factor 1	ctgacctgtgggggtcncctgccagacct
###	IRFex9_1	t/g	Verified	gene	n/a	Interferon regulatory factor 1	gccactccgactnctccaagagctg
###	IRFex9_2	t/g	Verified	gene	n/a	Interferon regulatory factor 1	tccatccacgttttttggcgtccactc
###	IRFpro1_1	a/g	Verified	gene	n/a	Interferon regulatory factor 1	gtagggtctatattttatggtt
###	IRFpro1_2	t/c	Verified	gene	n/a	Interferon regulatory factor 1	ggggcagggtaggcttctgcttNcttcacttcccc agggcaggtgagt
###	OCTex5_1	a/g	Verified	gene	n/a	carnitine transporter (organic cation transporter) 1	gaatacaaatatcacgtcgtgtacagctNgttgtca ttttgcagctttttgga
###	OCTN1ex1_1	g/c	Verified	gene	n/a	carnitine transporter (organic cation transporter) 1	gctgttagaaaattggggcgcgaaNccgggggacc gttcttgggaaaca

###	OCTN1ex3_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	gccctgagtcaggcatcaatgcagaNttagtgtttt tcagggtctgtgcag
###	OCTN1ex6_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	ggatatctgattccaggctcacttattatNttaccata gcagcaagacataatgg
###	OCTN1ex6_2	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	cttatgcatacactctcacttcaccttgac
###	OCTN1ex9_1	a/g		Verified	gene		n/a	carnitine transporter (organic cation transporter) 1	ctcagtcagtgtgacagatgttcctttgNtagagttc tttgcctaccagagttctc
###	OCTN2ex1_1	a/g		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	gtcgcgccccggctccagccccNagcgccgagaa gttgcgatgg
###	OCTN2ex3_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	accctgtcccccttgaggagacatcacagNtgtctcc agaaaggtaggtgatg
###	OCTN2ex3_2	a/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	tctcgtctcacagtgcctcatgcta
###	OCTN2ex4_1	a/g		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	gccagtgggcacatggggcacaNggtcacactc accaccaga
###	OCTN2ex4_2	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	actcaccaccagagtgccacgcacNagcaccccc ggcatcgtcagcgcc
###	OCTN2ex6_1	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	aactcccttaggcctgtcagtaaNaaatcagagtg aatgaaaatagga
###	OCTN2ex6_2	t/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	tatcctttcactctctgatgacaNaggcttgaatttg tctgaggg
###	OCTN2ex7_1	g/c		Verified	gene		n/a	carnitine transporter (organic cation transporter) 2	gcaagttaggagtatcaagcgaaaNccaaaata gccactgatatggtc

###	Polyex3_1	t/g		Verified	gene	n/a	Prolyl 4 hydroxylase	gctataagaggagaaacctttagagaggNtgaatg199 ggctggcctgttactcatg
###	Polyex6_1	t/c		Verified	gene	n/a	Prolyl 4 hydroxylase	ctatccagtggtcctcaggcttctccttgaagNgggaat ctcttccctaacca
###	Rad50ex16_1	ins/del	ins/del caa	Verified	gene	n/a	RAD50	tcctctgtatNaaagactgaa
###	Rad50ex16_2	other/w		Verified	gene	n/a	RAD50	
###	Rad50ex16_3	ins/del	ins/del t	Verified	gene	n/a	RAD50	agactgtctcNaaaaataaa ttaaataattNacaaaaaacat
###	Rad50ex25a_1	other/w		Verified	gene	n/a	RAD50	
###	Rad50ex4_1	t/c	ca repeat	Verified	gene	n/a	RAD50	atttaggaNccccccc ccttctgcittttaaaNttttctgttaaaaaag
###	Rad50ex4_2	t/c		Verified	gene	n/a	RAD50	ttaatggactacaagtNattttaagggttaacaa
###	Rad50ex7_1	a/t		Verified	gene	n/a	RAD50	gagattcttcatcaNacagaaaaatgtataacat
###	Sept2ex10b_1	a/g		Verified	gene	n/a	Septin-like	tctaaatatatttttgNcaccaggctcaagacaa
###	Sept2ex10c_1	a/g		Verified	gene	n/a	Septin-like	attaagactcccaagcNaatctctgcatattccaa
###	Sept2ex10d_1	t/c		Verified	gene	n/a	Septin-like	gtgtgtccacNgaggcacgg
###	Sept2ex10f_1	a/g		Verified	gene	n/a	Septin-like	tccctgttaagtNgggctcatgga
###	Sept2ex2_1	g/c		Not yet verified	gene	n/a	Septin-like	tgtcagggccctgNcctcagaca
###	Sept2ex3_1	t/c		Verified	gene	n/a	Septin-like	ccccagacctaNgacctccagga
###	TCF_1625	c/t		Verified	gene	n/a	t cell transcription factor 1	cactttgcctgcagggtgcaccgaaaaggacNtggg ggataaaatcaaaaaaagtgtgat

Table 4. Summary of best SNPs in chromosome 5 region.

	SNP marker name	Approximate Physical position ¹	SNP type	Transmitted allele	Frequency of allele ²	Transmitted	Untransmitted	C ²	p-value
5	IGR2055 a 1	435.0	G/T	G	0.357	87	39	18.29	0.000019
	IGR2060 a 1	437.5	C/G	C	0.351	81	34	19.21	0.000012
10	IGR2063 b 1	439.0	C/G	G	0.359	87	37	20.16	0.000007
	IGR2069 a 2	442.0	C/T	T	0.627	52	20	14.22	0.00016
	IGR2078 a 1	446.5	A/G	A	0.364	48	16	16.00	0.000063
15	IGR2096 a 1	455.5	A/C	A	0.349	75	32	17.28	0.000032
	IGR2198 a 1	506.5	C/G	G	0.364	87	41	16.53	0.000048
20	IGR2230 a 1	522.5	C/T	T	0.415	67	28	16.01	0.000063
	IGR2277 a 1	546.0	A/G	G	0.417	79	37	15.21	0.000096
	IGR3081 a 1	609.0	G/T	G	0.338	79	35	16.98	0.000038
25	IGR3096 a 1	616.5	C/T	C	0.429	89	42	16.86	0.00004
	PROLYL ex3 1	686.5	G/T	T	0.383	79	39	13.56	0.00023

¹ Position (kb) on the 850 kb reference sequence.30 ² Frequency of allele calculated from the untransmitted parental chromosomes.

TABLE 5

>IGR2001a

ggcccgaaaggactgtgccccctccccgtcaaacaccccccccccggtccccaccaag
ttctggccggggctgtggagcgtgggtcacctggggcggaaggactccacatcacggtga
agtggaggtgctgcagccccacaaagcccagaagcctgccaggggcgccccgggcgaa
cggcagtgggcggtgggcccgttctgcagcaccattggcgcgggggaggagagtgtgatc
ccatcaagccccgctccaggtcgcgccgctgggcctggcccaggagcctccccggcct
cggggcccatgggactgacagggggctgagttcttctcccaacggcggtgtttat
aagaaatgaagctccgcagcgccatcagcggcagcccacactgtcacccgccccgctc
tcaggggggttccggaacagccctgagcactggagcaattccttggtcagtattctatca
tgacccctagtatttccagccagcttcagcccacattctgcatttaggaattttat
aacagtgaacgtttattctgtgtcatacagcatatttgcacaaaccttgagaggg
gaggggctggtctggtgccccagtgtatctccagaaccaaacctgggggtcacaaaaag
caggcctgcgtgattcatatgtgtgaatgaattaaggga

>IGR2002a

cagccagcttcagccccacattctgcatttaggaattttataacagtgaacgtttattc
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From the foregoing, it is apparent that the invention includes a number of general uses that can be expressed concisely as follows. The invention provides for the use of any of the nucleic acid molecules described herein in the diagnosis or monitoring of diseases, particularly IBD, such as in the genotyping of samples from
5 individuals to be tested. The invention further provides for the use of any of the nucleic acid molecules in the manufacture of a medicament for the treatment or prophylaxis of such diseases. The invention further provides for the use of any of the nucleic acid molecules as a pharmaceutical.

While this invention has been particularly shown and described with references
10 to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the invention encompassed by the appended claims.